ABSTRACTS OF WORLD MEDICINE

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Pathology

286. **Electron Microscope Observations of the Platelet–Fibrin Relationship in Blood Clotting**
E. DE ROBERTIS. *Blood* [*Blood*] **10**, 528–533, May, 1955. 5 figs., 14 refs.

Most previous studies of blood platelets by electron microscopy have been concerned with the morphological changes which occur when the platelets come in contact with a foreign surface and with the disintegrating effect of thrombin on platelets. The present paper records observations made on the interaction of platelets with fibrin—the mechanism leading to clot retraction—made at the Institute of Biological Research, Montevideo. [For the technical details the original paper and the author's previous publication (De Robertis *et al.*, *Blood*, 1953, **8**, 587; *Abstracts of World Medicine*, 1954, **15**, 149) should be consulted.]

In the early stages of clotting morphologically intact platelets were shown to act as centres for the orientation and condensation of the threads of fibrin, but this was not so when the platelets had been damaged by the action of plasma from the splenic vein of a patient with idiopathic thrombocytopenic purpura. In the later stages of clot formation it was found that many platelets remain morphologically normal and attached to the fibrin, while others disintegrate. The relationship of these observations to clot retraction is discussed. [The article is illustrated with five excellent electron micrographs.] *A. S. Douglas*

EXPERIMENTAL PATHOLOGY

287. **The Effect of Poliomyelitis Virus on Human Brain Cells in Tissue Culture**
M. J. HOGUE, R. MCALLISTER, A. E. GREENE, and L. L. CORIELL. *Journal of Experimental Medicine* [*J. exp. Med.*] **102**, 29–36, July 1, 1955. 16 figs., 13 refs.

At the University of Pennsylvania, Philadelphia, the authors studied the cytopathogenic effect of poliomyelitis virus Type 1 (Mahoney) on cover-slip tissue cultures of human brain cells from 3 adults, 1 infant, and 3 foetuses. The virus was used in titres of 10^3, 10^4, and 10^6 infectious particles per ml. At the time of inoculation the age of the tissue cultures varied from 16 to 63 days.

Microscopical observation in a micro-slide incubator (at 37·5° C.) and photomicrography showed that the usual reaction of the neurones to the virus consisted in a contraction of the neurites and their withdrawal into the cell body, which became granular and then disintegrated. Vacuoles often developed in the neurones. The final contraction of the cell body and its change into a mass of granules were often very sudden. Variations of this pattern of reaction were observed; a terminal bulb often formed on the neurite, which was then partially or wholly drawn into the cell body, while in other instances the neurites were not withdrawn and remained intact long after the disintegration of the cell, eventually becoming fragmented or nodular, then granular, and finally disappearing. Foetal neurones often reacted within half an hour of inoculation, whereas adult neurones were less sensitive, reacting in 2 to 24 hours. The cells affected did not recover, and usually died within 3 days. Astrocytes, oligodendroglial cells, and macrophages were also affected, but reacted more slowly than the neurones. The effects of the virus were prevented by the addition of specific (monkey) antiserum or by preheating the virus. Uninoculated control tissue cultures remained in good condition. *Joyce Wright*

288. **Distribution and Absorption of Tobacco Tar in the Organs of the Respiratory Tract**
P. ERMALA and L. R. HOLSTI. *Cancer* [*Cancer (N.Y.)*] **8**, 673–678, July–Aug., 1955. 8 figs., 14 refs.

In the study here described from the University of Helsinki a full-scale plaster model of the human respiratory tract was made in two closely-fitting sections, a layer of egg-white being spread on the inner surfaces to simulate the mucosa of the organs. Smoke from a pipe or cigarette was then filtered through glass wool and intermittently drawn first into the oral cavity and then into the lungs by suction in the main bronchi. On separating the two sections the distribution of tar deposits was shown by their deep brown colour. To study the site and rate of tar absorption *in vivo* smoke was blown into the oral cavity and nostrils of mice, guinea-pigs, and one rhesus monkey. The animals were killed after 30 minutes, and sections of specimens from all parts of the respiratory tract were cut on a freezing microtome. The tar absorption at each site was measured by means of the fluorescence microscope.

A drawing shows the distribution of tar in the different regions of the model, and this is compared with a schematic summary of the clinical frequency of cancer at various sites in the human respiratory tract. A striking correlation is evident. Successive experiments showed that in pipe-smoking most of the tar condensed in the anterior part of the buccal cavity and little in the

lungs, while the reverse was true when cigarettes were smoked. Fractions of tobacco tars from pipe and cigarette smoke were collected over three temperature ranges, and showed distinct quantitative and qualitative differences. *H. G. Crabtree*

289. **Papillary Carcinoma of the Bladder in Mice, Obtained after Peroral Administration of Tobacco Tar**
L. R. Holsti and P. Ermala. *Cancer* [*Cancer (N.Y.)*] **8**, 679–682, July–Aug., 1955. 3 figs., 11 refs.

In a study carried out at the University of Helsinki the lips and oral cavity of 60 mice of a strain in which spontaneous tumours do not occur were painted daily (on 6 days a week) for 140 days with a tobacco tar. The 40 mice which survived for one year were then killed and their organs examined histologically.

The original aim of the study had been to examine the effect of tobacco tar on the buccal cavity. However, no malignant local changes were detected, but to the authors' surprise cancerous growths of the urinary bladder were revealed in many animals. Benign papillomatosis was found in 35 (87·5%) and papillary carcinoma of the urinary bladder in 6 (15%) of the animals surviving for one year. In two cases the growth had spread deeply into the surrounding tissues. No metastases were found. *H. G. Crabtree*

290. **Experimental Production of Carcinoma with Cigarette Tar. II. Tests with Different Mouse Strains**
E. L. Wynder, E. A. Graham, and A. B. Croninger. *Cancer Research* [*Cancer Res.*] **15**, 445–448, Aug., 1955. 8 figs., 7 refs.

291. **Analytical Pathology. II. Histopathologic Demonstration of Glomerular-localizing Antibodies in Experimental Glomerulonephritis**
R. C. Mellors, J. Arias-Stella, M. Siegel, and D. Pressman. *American Journal of Pathology* [*Amer. J. Path.*] **31**, 687–715, July–Aug., 1955. 30 figs., 30 refs.

At the Sloan-Kettering Institute and the Memorial Center for Cancer and Allied Diseases, New York, the role of glomerular-localizing antibodies in the pathogenesis of experimental glomerulonephritis has been studied by means of a technique for the histological demonstration of antibodies in tissues. This method was described in detail in a previous paper (*Lab. Invest.*, 1955, **4**, 69; *Abstracts of World Medicine*, 1955, **18**, 346) and consists in immunizing rabbits against ovalbumin, precipitating the antibody from the immune serum, and immunizing chicks against it. The chick antibody so produced is coupled to fluorescein, and unfixed frozen sections of rabbit tissues are treated with it, any resulting fluorescence in the section being taken to indicate the presence of rabbit antibody.

The authors induced glomerulonephritis in 12 of 15 rabbits by injecting bovine gamma globulin. The microscopic changes observed in the kidneys included glomerular capillary lesions, cellular proliferation, crescent formation, infiltration with polymorphonuclear leucocytes, and focal necrosis. Sections treated with chick-antibody–fluorescein conjugate were then photographed through a fluorescence microscope, the photomicrographs scanned with a densitometer, and the ratio of glomerular to tubular fluorescence calculated. In the kidneys of normal control animals and in kidneys in which only capillary changes were present this ratio averaged 1·4, but where there was cellular proliferation or crescent formation it was 2·0 to 2·1.

This increased glomerular fluorescence is held by the authors to indicate the localization of antibody in the glomeruli, presumably due to previous fixation there of some of the injected foreign protein antigen, and hence to provide support for the theory that glomerulonephritis is an allergic condition. They suggest that this method should prove useful in studying the pathogenesis of glomerulonephritis and of other diseases of possible allergic aetiology in man.

[In the abstracter's opinion the implications of this work are by no means clear. The authors did not exclude the possibility that the chick antibody to rabbit antibody-globulin might also react with other rabbit globulins, so that all they have demonstrated is a glomerular accumulation of globulin, not necessarily antibody, in experimental glomerulonephritis. The significance of the ratios of glomerular to tubular fluorescence given is difficult to evaluate, since some of the photomicrographs reproduced show considerable fluorescence, presumably non-specific, in the tubules, while others show little; moreover, the value given in this paper as the ratio for normal kidney tissue (1·4) differs considerably from that given in the authors' previous paper (0·9). Further, if the glomerulitis is due to an antibody-antigen reaction *in situ* it is not clear why antibody is not found in the glomeruli in the stage of capillary damage, but only when more advanced lesions are present. Finally, the validity of the authors' conclusion that increased glomerular fluorescence is due to localization of antibody—with all that this implies regarding the pathogenesis of glomerulonephritis—must be regarded as dubious in view of their statement that increased glomerular fluorescence was also found in lipid nephrosis and secondary amyloidosis.]

M. C. Berenbaum

292. **Studies on the Ameba–Bacteria Relationship in Amebiasis. Comparative Results of the Intracecal Inoculation of Germfree, Monocontaminated, and Conventional Guinea Pigs with *Entamoeba histolytica***
B. P. Phillips, P. A. Wolfe, C. W. Rees, H. A. Gordon, W. H. Wright, and J. A. Reyniers. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 675–692, July, 1955. 9 figs., 22 refs.

In a study carried out at the National Institutes of Health, Bethesda, Maryland, bacteria-free guinea-pigs were obtained from gravid females by Caesarean section and reared with all sterile precautions. Some of these animals were then infected with the Shaffer–Frye "streptobacillus", with *Escherichia coli*, or with *Aerobacter aerogenes*. The bacteria-free guinea-pigs and those harbouring a single bacterial species were inoculated intracaecally with an invasive strain (Strain 200) of

Entamoeba histolytica. The cultures of amoebae were obtained by isolating cysts from a culture with mixed bacteria which were then hatched in a culture with *Trypanosoma cruzi*. The *E. histolytica–T. cruzi* cultures were used for inoculation of guinea-pigs within 2 weeks of isolation, since previous work had shown that after this time the virulence is lost. The animals, which were then 14 to 21 days old, received about 300,000 amoebae in a volume of 1 ml. They were killed and examined at intervals of 1 to 33 days after inoculation, and if no amoebae could be found microscopically, material from the caecum and colon was cultured. The possibility of bacterial contamination of the animals was checked by making examinations weekly and at the end of the experiment.

The results showed that in the 35 bacteria-free inoculated guinea-pigs the amoebae survived for only 5 days, animals kept for longer periods having invariably lost their infection. Infection with the Shaffer–Frye streptobacillus (20 animals) extended the survival of amoebae to 8 days. However, in these animals the growth of the bacteria in the intestine was very poor, being detectable only by cultivation. In both groups of animals examination of sections of the intestinal wall revealed no microscopic lesions. These results were in great contrast with those seen in the guinea-pigs infected with *E. coli* or *A. aerogenes*. Out of 7 *E. coli*-infected animals inoculated with *Entamoeba histolytica*, 6 developed ulceration, while the seventh was harbouring many amoebae at 11 days. All 5 animals infected with *A. aerogenes* and inoculated with *E. histolytica* showed ulceration at necropsy. As controls, 3 guinea-pigs infected with *E. coli* and 2 with *A. aerogenes* were observed for 20 days; at necropsy no lesions were seen, nor were any found on microscopical examination of sections of the intestinal wall; the bacteria alone, therefore, did not produce ulceration. The *Entamoeba histolytica–T. cruzi* cultures were also inoculated into guinea-pigs born and reared in the normal manner. Out of a total of 66 animals, ulceration was found in 59 and 6 showed the presence of amoebae in the intestinal lumen.

The histological picture of the amoebic ulceration in the animals harbouring *E. coli* or *A. aerogenes* was similar to that found in control animals. However, the epithelial layer of the caecal glands seemed to have offered more resistance to amoebic penetration; this was more especially seen in animals infected with *E. coli* than in those with *A. aerogenes*. In both cases there were fewer points of entry in the mucosa and such areas were limited to a few cells. Having penetrated, however, the amoebae destroyed underlying tissue, particularly connective tissue, as deep as the muscularis mucosa and then spread laterally. Inflammatory reaction accompanied ulcer formation. These experiments clearly show that amoebae alone cannot infect the gut of bacteria-free animals and that the presence of certain bacteria is necessary for the full development of the invasive capacity of the amoebae.

[This is a very important paper, since the authors have applied an entirely new technique to the experimental study of amoebiasis.] *R. A. Neal*

CHEMICAL PATHOLOGY

293. **Uropepsin as a Measure of Gastric Secretion**
S. P. RIGLER, H. A. OBERHELMAN, M. M. HANKE, and L. R. DRAGSTEDT. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **71**, 63–67, July, 1955. 8 refs.

In this contribution to the study of the pathogenesis of peptic ulceration the uropepsin excretion, nocturnal acid secretion, and the peptic activity of the gastric juice were determined in three groups of patients investigated at the University of Chicago Hospitals: (1) 16 patients admitted with a diagnosis other than peptic ulcer, who acted as a control group; (2) 29 patients with duodenal ulcer (confirmed by subsequent operation); (3) 23 patients who had undergone vagotomy 6 months to 8 years previously for duodenal ulcer and who were symptom-free at the time of investigation.

In Group 1 the mean acid secretion was 16 mEq. HCl (standard error ±4·8), the mean gastric peptic activity was 29,706 (±5,436) "peptic units" per hour, and the mean uropepsin excretion 142 (±36) peptic units per hour. In Group 2 the corresponding values were 48 (±4·7) mEq. HCl, 62,824 (±6,331) peptic units per hour, and 146 (±23) peptic units per hour. In this group the amount of acid secreted in most cases varied directly as the peptic activity, but neither was correlated with uropepsin excretion. Uropepsin was absent in 5 cases, was less than 50 peptic units per hour in 5 cases, and exceeded 50 units per hour in 19 cases. In Group 3, acid secretion was 7·6 (±2·5) mEq., gastric pepsin was 19,047 (±2,890) peptic units per hour, and uropepsin excretion was 97 (±21) peptic units per hour. Here too the amounts of acid and pepsin secreted were correlated, but that of uropepsin varied independently of either.

The authors conclude that uropepsin excretion is independent of gastric secretory activity as measured by nocturnal acid output and gastric peptic activity, and that peptic ulceration is due to hypersecretion of vagal origin. They suggest that the finding of increased uropepsin excretion in some patients with duodenal ulcer is incidental and the result of stress, and that this finding does not warrant the assumption that such increased secretion is concerned in the causation of the lesion. *M. Lubran*

294. **The Significance of Paper Electrophoresis of Serum Lipids in the Investigation of Liver Disease.** (Die Bedeutung des papierelektrophoretischen Lipidogrammes für die Beurteilung von Leberkrankheiten)
F. H. FRANKEN and E. KLEIN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 1074–1077, July 22, 1955. 37 refs.

At Bad Cannstatt Hospital, Stuttgart, the authors have studied by paper electrophoresis the serum protein pattern in 30 cases of hepatitis (24 acute and 6 chronic), 13 cases of cirrhosis of the liver, 3 of obstructive jaundice, and 3 of carcinomatosis of the liver. The filter-paper strips were divided and stained selectively to show the position and proportion of the protein fractions and of

the lipoproteins respectively. The results were remarkable in that in all types of liver disease except chronic hepatitis the lipoprotein fraction in the position of the α_1 globulin was either absent or considerably decreased; in the sera from patients with chronic hepatitis the α_1-lipoprotein fraction was slightly increased. The authors therefore conclude that the examination of lipoproteins by paper electrophoresis is of no help in the differential diagnosis of obstructive jaundice, carcinomatosis of the liver, hepatic cirrhosis, and acute hepatitis, but that it is of help in the recognition of chronic hepatitis. *H. Lehmann*

295. **A Short Laboratory Screening Test for Phaeochromocytoma**
R. MOULTON and D. A. WILLOUGHBY. *Lancet* [*Lancet*] **2**, 16–18, July 2, 1955. 1 fig., 13 refs.

The authors describe a new screening test for the detection of phaeochromocytoma in patients with sustained hypertension. The method depends on the detection of excessive urinary excretion of adrenaline and noradrenaline by observing the effect on the blood pressure of injection of the patient's untreated urine into the anaesthetized cat.

In an extended trial of the test with the urine of 250 hypertensive patients the great majority of samples had little or no effect on the cat's blood pressure. When a rise occurred indicating an amount of adrenaline or noradrenaline in the urine greater than 0·1 μg. per ml., further tests were performed, the pressor effect being studied after treatment of the urine sample with sodium hydroxide and ferric chloride, which destroys adrenaline. The potentiating effects of ergotamine tartrate, mepyramine maleate, and dibenzylene were also determined and helped to establish that the pressor substance was indeed adrenaline.

In all 7 cases of phaeochromocytoma detected in the series the urinary output of pressor amine was increased, being more than 1·0 mg. daily in 6. (The normal output is less than 60 μg. per 24 hours.) In several cases of essential hypertension outputs two to three times greater than normal were found, but in none of these borderline cases did repeated assays reveal the presence of a phaeochromocytoma. The test is now carried out as a routine in the authors' clinic at University College Hospital, London, and so far no false positive or false negative results have been encountered. *C. L. Cope*

296. **A Rapid Test for Occult Blood in the Faeces**
V. P. FIRTH. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 130–134, 1955. 3 refs.

The rapid test for occult blood in faeces first proposed by Gregersen in 1919 and later slightly modified by Needham and Simpson (*Quart. J. Med.*, 1952, **21**, 123; *Abstracts of World Medicine*, 1952, **12**, 298) involves the application of a reagent containing benzidine hydrochloride and barium peroxide in glacial acetic acid directly to an unboiled faecal smear on a glass slide or filter paper. The present author has compared the results of this test with those obtained by using standard methods in the examination of 71 specimens from 44 patients. Agreement with the standard tests was obtained in 91% of the specimens. He also showed that the accuracy of the test could be further increased by performing it on boiled faeces when the unboiled specimen gave a weakly positive result. *H. Harris*

MORBID ANATOMY AND CYTOLOGY

297. **Congenital Cerebral Aneurysms**
R. R. WILLIAMS, R. C. BAHN, and G. P. SAYRE. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **30**, 161–168, April 20, 1955. 2 figs., 9 refs.

At the Mayo Clinic and the State Hospital, Rochester, New York, a study was made of 172 congenital cerebral aneurysms found at necropsy in 143 patients between 1924 and 1950. In 24 patients the aneurysms were multiple, 5 being identified in one patient, 4 in one, and 2 each in 22 patients. The incidence was highest in the age group 40 to 59 years; the youngest patient in the series was 18 and the oldest 89 years of age. There was no significant difference in the sex distribution. The aneurysm was most frequently found on the anterior cerebral arteries and the anterior communicating artery (37%); nearly 80% of these were at the junction of the anterior cerebral artery with the anterior communicating artery or were on the anterior communicating artery itself. The second most common site was the internal carotid artery (32%). Of the 172 aneurysms, 94 had ruptured, causing death of the patient; 78 were unruptured and were an incidental finding at necropsy. The incidence of ruptured aneurysms was highest in patients in the sixth decade. There did not appear to be any significant relationship between the size of the aneurysm and the incidence of rupture. Haemorrhage extended into the brain substance in 57 cases, involving the ventricles in 43. Of the patients with ruptured aneurysm, one-third died within 48 hours of the onset of symptoms of subarachnoid haemorrhage and one-third during the next 10 days; in the remainder, who survived 2 weeks or longer, cerebral haemorrhage was the commonest cause of death. *Ruby O. Stern*

298. **Arteriosclerotic Occlusion of Cerebral Arteries: Mechanism and Therapeutic Considerations**
W. L. BRUETSCH. *Circulation* [*Circulation* (*N.Y.*)] **11**, 909–913, June, 1955. 4 figs., 12 refs.

To elucidate the exact mechanism of occlusion of the cerebral arteries the brains of 20 patients with cerebral arteriosclerosis and encephalomalacia were examined histologically at Indiana University, Indianapolis. No evidence of true arterial thrombosis was found, although vascular occlusion was often noted, resulting from an atheromatous plaque (in the larger arteries) or endothelial proliferation (in small arteries and arterioles). The author's observations suggest that in the genesis of the atheromatous plaque the lipid deposits are of secondary importance, and that the primary mechanism is one of fibroblastic proliferation. The " embryonic foci of

cellular proliferation" seen in the fibrous portion of many plaques are, he believes, the source of the slow fibroblastic proliferation which occurs in the large cerebral arteries as in the coronary arteries. In these foci the predominant cells are young fibroblasts, lymphocytes, and undifferentiated mesenchymal cells, sometimes showing amitotic division. It is suggested that the endothelial proliferation in small vessels and the foci of fibroblastic proliferation in the plaques within larger arteries are evidence of a morbid process recurring at a time of life when various cell types show a great propensity for abnormal growth. The use of drugs which inhibit cell division and others which delay connective tissue formation may be advantageous in retarding the arteriosclerotic process. *John N. Walton*

299. **Smears from the Oral Mucosa in the Detection of Chromosomal Sex**
K. L. Moore and M. L. Barr. *Lancet* [*Lancet*] **2**, 57–58, July 9, 1955. 3 figs., 14 refs.

In the determination of chromosomal sex by the examination of a skin biopsy specimen difficulty is sometimes encountered in obtaining sections showing sufficiently fine nuclear detail. In a study carried out at the University of Western Ontario, London, Ontario, the authors have investigated the use of smears from the oral mucosa. From 140 persons (81 males and 59 females) aged from 2 days to 62 years smears were obtained by rubbing the mucosa of the cheek firmly with the edge of a wooden tongue depressor. These were then fixed in Papanicolaou's fluid (equal parts of 95% ethyl alcohol and ether) and stained with cresyl echt violet.

The characteristic female sex chromatin was visible in the nuclei of epithelial cells of females, whereas no similar chromatin mass was observed in the nuclei of male cells. The sex chromatin of female cells is thought to be formed by heterochromatic portions of the two X chromosomes adhering to each other in intermitotic nuclei; the XY sex chromosomes of male nuclei do not form a distinctive mass of chromatin. This sex difference in nuclear morphology, which has also been observed in several other mammals, has been used as an aid in the differential diagnosis in cases of aberrant sex development, such as hermaphroditism and gonadal dysgenesis. The authors have found the examination of smears of oral mucosa to be a reliable alternative to the method of skin biopsy, and point out that it has the advantage of simplicity. *R. J. Ludford*

300. **The Blood-supply of the Human Thyroid Gland under Normal and Abnormal Conditions**
N. Johnson. *British Journal of Surgery* [*Brit. J. Surg.*] **42**, 587–594, May, 1955. 12 figs., 12 refs.

Summarizing the results of his earlier studies of the minute vascular anatomy of the human thyroid gland the author, in this paper from the University of Melbourne, reasserts that the thyroid lobule, consisting of 20 to 40 vesicles, is the unit of structure of the thyroid gland. It receives its own lobular artery, which breaks up into a series of twigs passing to the vesicles, each of which has its own capillary plexus. Anastomoses occur between lobular arteries just before they enter the lobule. Arterio-venous communications may be found in thyrotoxicosis, but as yet there has been no direct evidence of this in the human subject.

The thyroid nodule has a vascular supply identical with the lobule and may, as it increases in size, develop thin-walled sinusoids as a modification of the existing capillary bed. Haemorrhage and necrosis in thyroid nodules may be sequelae if these channels produce an intranodular arterio-venous shunt. *Guy Blackburn*

301. **Occult Sclerosing Carcinoma of the Thyroid**
G. H. Klinck and T. Winship. *Cancer* [*Cancer* (*N.Y.*)] **8**, 701–706, July–Aug., 1955. 8 figs., 7 refs.

In 1949 Hazard *et al.* (*J. clin. Endocr.*, **9**, 1216) reported 25 cases of non-encapsulated sclerosing tumours of the thyroid gland and expressed the view that until more was known of their natural history these tumours "should not be regarded as true carcinoma". In consequence of this the present authors have investigated 32 further similar cases (the largest series so far) taken from the files of the Armed Forces Institute of Pathology, Washington, D.C., and suggest that these tumours appear to form a distinct sub-group of malignant thyroid tumours; they occurred in 22 women and 10 men. The lesions measured from 0·3 to 0·9 cm. in diameter, were all situated at the outer periphery of the gland, and appeared macroscopically to be small scars, frequently having a scalloped outline. Microscopically they were seen to consist of foci of scirrhous adenocarcinoma, occasionally displaying a papilliferous structure, and had invaded the adjacent thyroid tissue in two-thirds of the cases. In one case there were two independent lesions, while in another the growth had penetrated the thyroid capsule to invade the skeletal muscles.

The thyroid glands in these cases exhibited a variety of changes ranging from involution to hyperplasia, but in none of the patients with metastases were signs of hyperthyroidism recorded. In 8 cases the presence of the tumour had been entirely unsuspected and an enlarged, metastatic, cervical lymph node was the first evidence of the neoplasm. Although these tumours occurred in patients of all ages after the first decade, the average age of those without metastases was 35 years, as compared with 45 years for those with metastases to the cervical nodes; the authors interpret this as suggesting that the growth is slow to metastasize. Four of the patients were known to have died from unrelated causes. Only 7 of the remaining 28 could be traced, but all these were alive and well, one patient with metastases 2½ years after operation, and 6 without metastases after 1 to 7 years. The authors suggest that these tumours should be designated "occult sclerosing carcinoma of the thyroid gland". *R. Salm*

302. **The Diagnosis of Esophageal Carcinoma by Exfoliative Cytology, Including Two Cases of Cardiospasm Associated with Carcinoma of the Esophagus**
M. I. Klayman. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 33–44, July, 1955. 6 figs., 11 refs.

303. **A Clinical Pathological Study of the Newborn Lung with Hyaline-like Membranes**

E. F. LATHAM, R. E. L. NESBITT, and G. W. ANDERSON. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 173–198, May, 1955. 3 figs., 16 refs.

The authors have attempted to correlate the obstetric history with the post-mortem findings in a number of cases in which hyaline-like membrane was present in the lungs of infants dying in the early neonatal period. Between 1937 and 1949, 26,213 babies weighing over 1,000 g. were born alive at the Johns Hopkins Hospital, Baltimore, with 480 neonatal deaths. Necropsy was performed in 407 of these cases, and in 124 (30·5%) a pulmonary hyaline-like membrane was found. It was twice as frequent in premature infants (1,000 to 2,499 g.) as in those whose birth weight was 2,500 g. or more. No example was found among 563 stillborn babies examined. (Babies weighing 400 to 999 g. at birth were excluded from the present analysis, but it is noted that among 52 cases of neonatal death in this category the incidence of pulmonary membrane was 25%.) An arbitrary system of grading according to the thickness and distribution of the membrane was adopted, four grades being recognized and 90% agreement in grading being attained by three observers working independently. Cases placed in Grade I, with scattered, irregular, thin membranes in a few alveolar ducts and alveoli only, differed from those in Grades II, III, and IV in that the degree of atelectasis present, determined by estimating "the percentage of area of lung to the area of the alveolar spaces", never reached the critical level of 70%, above which it was considered to constitute a possible cause of death *per se*.

On histological grounds the 407 cases were grouped as follows: (A) 283 cases with no membrane; (B) 124 cases with membrane; (C) 60 cases from Group B with Grade-I membrane and less than 70% atelectasis; (D) 64 cases from Group B with membrane of Grade II, III, or IV and at least 70% atelectasis; (E) 42 cases from Group D where no other possible cause of death was present. The incidence of membrane was 4·7 per 1,000 live births, and of membrane with at least 70% atelectasis 2·4 per 1,000. A comparison of the incidence of various complications of labour and delivery in Groups A and B showed an increased risk of membrane formation to be associated only with Caesarean section (such births providing 27% of the cases with membrane). Of 11 infants born of diabetic mothers, membrane was present in 5. Prematurity was associated with an incidence of membrane 6·9 times greater than the expected figure—there were only 2 babies in Group D and none in Group E whose birth weight was above 3,000 g. On the other hand one-third of the babies born by Caesarean section in whose lungs membrane was found were born at term. No definite correlation between membrane formation and the use of anaesthesia or analgesia in labour was observed. The condition of the infant at birth was excellent in 60% of cases in Group B.

The average period of survival in Group B was 30 hours, 62% of the babies dying in the first 24 hours, but whereas some in Group C survived up to 30 days, all the infants in Groups D and E died within 6 days. There was an inverse relation between the length of survival and the extent of membrane. In 29 cases an inflammatory reaction (pneumonitis) was found, and these infants survived longer than the others. From a study of these cases the authors conclude that the risk of infection is greater when the foetal membranes have ruptured 3 or more days before delivery, there being 4 such cases among the 29 with pulmonary infection and only 2 among the 95 without.

In only 30% of cases in Group B (8·6% of all neonatal deaths) did the presence of 70% or more atelectasis suggest that this in itself was the probable cause of death. However, it is the authors' opinion that "hyaline-like membrane in conjunction with other pulmonary pathology" is responsible for a large proportion of the neonatal deaths attributable to "abnormal pulmonary ventilation". The relative importance of the membrane in any particular case can be assessed only by a study of all the clinical and pathological factors involved.

A. White Franklin

304. **The Histology of Lung Cancer**

J. B. WALTER and D. M. PRYCE. *Thorax* [*Thorax*] **10**, 107–116, June, 1955. 12 figs., 30 refs.

The difficulties presented by the histological classification of malignant epithelial tumours of the lung are discussed and the differences in distribution of cases among the various categories in published series are cited as indicating the need for more precise criteria for the identification of each type of tumour. On the basis of the histological findings 207 surgical specimens and 159 necropsy specimens from a number of London hospitals were classified by the authors as follows:

Type of Growth	Surgical Series		Necropsy Series	
	No. of Cases	%	No. of Cases	%
Oat-cell carcinoma ..	33	15·9	59	37·1
Squamous-cell carcinoma	125	60·4	32	20·1
Adenocarcinoma ..	32	15·5	45	28·3
Polygonal-cell carcinoma	16	7·7	17	10·7
Metastasizing "adenoma"	1	0·5	—	—
Unrecognizable owing to poor histology ..	—	—	6	3·8

Their definition of the oat-cell growth is clearly expounded, the characteristic feature being described as "the relatively small cells with round, oval, or oat-shaped hyperchromatic nuclei and scanty, ill-defined cytoplasm".

A. C. Lendrum

305. **The Site of Origin of Lung Cancer and its Relation to Histological Type**

J. B. WALTER and D. M. PRYCE. *Thorax* [*Thorax*] **10**, 117–126, June, 1955. 8 figs., 20 refs.

The histological classification of the series of malignant tumours of the lung described in the previous paper [see Abstract 304] is here correlated with their distribution according to site and size, the standards adopted being clearly defined. Squamous-cell growths were found to

be more often central in origin, adenocarcinomata always peripheral, and the other types evenly distributed. In the surgical series most of the smaller tumours were centrally and the larger peripherally situated, suggesting that the central type produces symptoms at an earlier stage. About half the surgical specimens were peripheral, although comparison of the two series definitely indicated that the central type is favoured for resection. The authors therefore conclude that more than half of all pulmonary cancers are peripheral, and that this is one of the major factors responsible for the low operability and poor prognosis of these tumours.

A. C. Lendrum

306. **The Healed Primary Complex in Histoplasmosis**
M. STRAUB and J. SCHWARZ. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **25**, 727–741, July, 1955. 10 figs., 28 refs.

In the city of Cincinnati, Ohio, the reaction to the histoplasmin test is positive in some 50% of the negro and 70% of the white population. Of 105 unselected necropsies performed at the Cincinnati General and Jewish Hospitals healed pulmonary lesions of histoplasmosis were found in 70 (15 out of 30 on negro and 55 out of 75 on white subjects); these lesions were often calcified and bore a striking resemblance to the primary complex of tuberculous disease, though both the pulmonary focus and the affected related lymph nodes were commonly larger than in tuberculosis. Although the infection is generally subclinical, splenic lesions in 19 of the cases were proof of dissemination. The organisms were demonstrated, often in large numbers, in sections of calcified and ossified masses, but 40 attempts at culture were unsuccessful. *A. C. Lendrum*

307. **The Pathology of the Adrenals, Thymus and Certain Other Endocrine Glands in Addison's Disease: an Analysis of 37 Necropsies**
J. C. SLOPER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 625–628, Aug., 1955. 19 refs.

In order to obtain further information regarding the incidence and severity of the pathological changes in the endocrine glands in Addison's disease, the author has reviewed the records of 37 cases of this disease coming to necropsy at the London Hospital between 1912 and 1951. The study showed that in 15 of these there was idiopathic atrophy of the adrenal glands and in 22 granulomatous and fibrocaseous tuberculosis of the glands; care was taken to exclude simple atrophy characteristic of Simmonds's disease. In the idiopathic group the adrenal medulla was normal, whereas in the tuberculous group medullary tissue was absent in 18 cases and scanty in 4. The surviving adrenocortical tissue was markedly less in the tuberculous group than in the idiopathic group.

There was no clear-cut hypertrophy of the thymus gland, although the observations did not preclude the possibility of it. Hyperplasia of the islet cells of the pancreas was not confirmed, but the pancreas tended to be diminished in weight, and in one case in which diabetes mellitus was also present there was atrophy of the pancreas. In both types of Addison's disease the number of basophil and acidophil cells in the anterior lobe was reduced, while that of chromophobe cells was increased. In 7 out of 11 cases of the idiopathic form of the disease investigated there was abnormal involution of the thyroid gland, whereas this abnormality was seen in only 2 cases out of 10 examined in the tuberculous group. Analysis of the findings led to the conclusion that only the adrenal and pituitary glands are constantly affected in Addison's disease. It is suggested that the finding of a tendency towards involution of the thyroid gland in idiopathic cases, and the greater destruction of adrenal tissue, particularly the medullary portion, in tuberculous cases, may be helpful in differentiating the two types of Addison's disease. *P. A. Nasmyth*

308. **A Histochemical Study of Epidermal Glycogen in Skin Diseases**
K. STEINER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 599–618, June, 1955. 18 figs., 32 refs.

One hundred cases of 30 different skin diseases were examined for epidermal glycogen. The standard method used was the McManus stain for polysaccharides, controlled by diastase.

Considerable amounts of glycogen were found in psoriasis, in some acute types of dermatitis, in cases of pemphigus vulgaris and dermatitis herpetiformis, in circumscribed pretibial myxedema, in cornu cutaneum, in the surface epithelium of epitheliomas, and in some keratinized papillomas; moderate amounts in lichen planus, in discoid lupus erythematosus, in scleredema, in keratinizing acuminate condylomas, in prickle cell epitheliomas, and in the prickle cell portions, and squamous sheets and pearls, of mixed epitheliomas. In all these instances the glycogen was usually present in the middle layers, or in the upper layers, of the Malpighian rete, never in the basal cells. It was almost always in collections of small granules. Parakeratotic layers contained often glycogen. Particularly in premalignant and malignant lesions there were also polysaccharides other than glycogen, especially in the keratogenous zone. This mixture of polysaccharides appeared usually more diffuse than glycogen.

Small amounts of glycogen were present in some verrucae, in senile keratoses, in some papillomas, in chronic eczemas, in erythrodermias, in some cases of discoid lupus erythematosus, in sclerodermas, and in pseudo-epitheliomatous hyperplasia. The following lesions were completely glycogen-negative: calluses, most verrucae, most papillomas, basal cell epitheliomas, the majority of sclerodermas, some cases of pemphigus vulgaris and dermatitis herpetiformis, urticaria pigmentosa, mycosis fungoides, pseudoxanthoma elasticum and cutis hyperelastica.

In general, considerable glycogen was found in parakeratotic processes, rarely in hyperkeratotic lesions. No constant correlation between acanthosis and glycogen could be found. It is concluded that, in skin diseases, glycogen is present whenever there is abnormal keratinization.—[Author's summary.]

Microbiology and Parasitology

309. **Production of Poliomyelitis Virus with Combined Antigenic Characteristics of Type I and Type II**
K. SPRUNT, I. M. MOUNTAIN, W. M. REDMAN, and H. E. ALEXANDER. *Virology* [*Virology*] **1**, 236–249, July, 1955. 1 fig., 13 refs.

The induction of genetic changes in poliomyelitis virus, if feasible, would appear to be a more efficient means of obtaining mutant strains with desired combinations of heritable properties than the search for rarely occurring spontaneous mutants. In the experiments here described from the Babies Hospital (Columbia University), New York, the method used for the induction of such changes was that of " double infection ", monkey kidney tissue-culture cells being infected simultaneously with two different strains of virus, thus allowing interaction between the nucleic acids of the two strains within the cell.

The strains used were the Mahoney (Type I) and MEF I (Type II) viruses, and the inocula were so adjusted in size that in each culture tube there were 10 infectious units of each virus to every cell of the culture. After 3 hours' incubation the residual virus was removed, the cells washed three times, and a maintenance fluid added. When the maximum degree of cell destruction had occurred, after 24 to 40 hours' incubation, the supernatant fluid from each tube was removed and those in which the two parent types of virus were present in approximately equal proportions were examined for the presence of " combined " particles capable of being neutralized by both Type-I and Type-II antisera. The presence of such particles was inferred when the titre of cytopathogenic activity of the fluid measured in the presence of normal monkey serum was considerably greater than the sum of the titres measured in the presence of Type-I and Type-II antisera, suggesting that each antiserum had neutralized more than the homotypic virus.

The " combined " virus was considered to be present predominantly in one out of 5 tubes tested and has so far been carried through a few passages at limiting dilution, although still accompanied by one or other of the parent types of virus, thus indicating that the " combined " particle is probably not stable.

J. E. M. Whitehead

310. **Semi-solid Agar Media for Rapid Culture of Tubercle Bacilli**
R. KNOX. *Lancet* [*Lancet*] **2**, 110–112, July 16, 1955. 1 fig., 9 refs.

Some preliminary experiments with semi-solid agar media for the culture of tubercle bacilli are reported from Guy's Hospital, London. Agar in a final concentration of 0·1 to 0·125 g. per 100 ml. was added to Kirschner's and to Dubos's media; horse serum (final concentration 10%) was then added to the former and bovine albumin Fraction V (0·35%) and " tween 80 " (0·05%) to the latter. These media were inoculated with: (1) *Mycobacterium tuberculosis* var. *hominis* H37Rv and variants of this strain made resistant to isoniazid or streptomycin; (2) a strain of B.C.G. and an isoniazid-resistant variant; and (3) NaOH concentrates of selected microscopically positive sputa from tuberculous patients. Drug-sensitivity tests with isoniazid and streptomycin were undertaken with pure cultures of tubercle bacilli and with sputum concentrates. Incubation was aerobic at 37° C.

Profuse and rapid growth of tubercle bacilli was consistently obtained on both media. With large inocula growth was easily visible in 2 to 3 days, while with small inocula discrete colonies could be counted in 7 to 10 days. The author points out that agar in a concentration of 1 to 2% is often highly inhibitory to tubercle bacilli, but in a concentration of 0·1% it permits rapid growth of the bacilli. Moreover, quantitative studies, not possible with liquid media, were carried out, including rapid viable counts, drug-sensitivity tests, and estimation of the proportion of drug-resistant organisms present in a culture.

The value of the media in routine primary culture of clinical specimens is to be the subject of a further investigation.

Joyce Wright

311. ***para*-Aminosalicylic Acid in Sputum. II. Elimination of Its Effects on Culture for Tubercle Bacilli**
D. YEGIAN, V. BUDD, and J. BALA. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 860–866, June, 1955. 6 refs.

Occasionally, microscopical examination of sputum from tuberculous patients reveals the presence of acid-fast bacilli, yet the organisms fail to grow in cultures of the same specimen. This was observed at Ray Brook State Tuberculosis Hospital, New York, in 1·5% of specimens examined before the advent of chemotherapy and later in 22% of specimens from patients receiving streptomycin–PAS therapy. This increase was attributed to contamination of the sputum with PAS retained in the mouth, and when, as a routine, patients rinsed the mouth with water after taking PAS the incidence fell to 8·6% (101 of 1,173 specimens). By incorporating a small amount of *para*-aminobenzoic acid (PABA) in one of the culture tubes it was possible to obtain growth of tubercle bacilli from 38 specimens which had failed to yield the organisms on the usual media. When culture on this medium proved negative, re-inoculation of scrapings from the culture tubes gave positive results for 8 further specimens, thus reducing the percentage of specimens which were negative on culture but positive on microscopy to 4·7, and most of these specimens were in the low Gaffky range.

The authors state that the incorporation of PABA in solid medium has disclosed strains of tubercle bacilli which are sensitive to this drug, but that so far this

has only been observed in strains which are resistant to streptomycin, PAS, or isoniazid, or to a combination of these drugs. *E. G. Rees*

SEROLOGY AND IMMUNOLOGY

312. **The Formation of Antibody: a Study of the Relationship between a Normal and an Immune Haem-agglutinin**

K. B. FRASER. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **70**, 13–33, 1955. 4 figs., 23 refs.

Evidence is provided in this paper from the University of Aberdeen that the T-agglutinin normally present in the serum of man and the rabbit is an ill-defined mixture of antibody molecules, differing notably in specificity and avidity. The major part is non-specific for human, sheep, horse, and guinea-pig erythrocytes treated with receptor-destroying enzyme ("treated" erythrocytes), but small fractions are specific for treated erythrocytes of all four species.

Immunization of rabbits with treated erythrocytes of these four species leads to great changes in the distribution of T-agglutinin. Two types of immune body occur: one is a completely specific warm-temperature agglutinin, appearing early in the process of immunization; the other has the character of an altered normal T-agglutinin, acting as a non-specific warm-temperature agglutinin to homologous cells, and as a non-specific low-temperature agglutinin to heterologous cells. After cessation of immunization, the modified T-agglutinin may revert to its normal character.

The author considers that in this instance immunization with treated erythrocytes involves the production of modified T-agglutinin, and therefore modification of the antibody-producing sites in which T-agglutinin was synthesized before immunization. In his view these experiments support the adaptive-enzyme hypothesis of antibody production put forward by Burnet. [This is a complex and difficult paper, almost impossible to abstract adequately. It will amply repay very detailed examination by those interested in the theories of antibody synthesis.] *C. L. Oakley*

313. **Studies in Leukemia. I. Etiologic Mechanism: Antigen–Antibody Techniques. II. Comparison of Slide and Test Tube Techniques for Agglutination Studies with Guinea-pig Serum.** [In English]

H. M. SCHOOLMAN, S. O. SCHWARTZ, and W. SPURRIER. *Acta haematologica* [*Acta haemat.* (*Basel*)] **14**, 1–6 and 7–10, July, 1955. 4 refs.

Following the observation of Kidd that normal guinea-pig serum contained some protective factor against transplanted mouse lymphoma the present authors have investigated immunologically the properties of normal guinea-pig serum. They found that the serum of normal adult guinea-pigs gave strong agglutination and precipitin reactions with leukaemic AKR mouse tissues, but that the serum of young guinea-pigs did not contain this factor; further, no reactions were noted with the tissues of normal AKR mice. The guinea-pig serum factor was found to resist heating to 56° C. for 30 minutes and freezing for 12 days; it could not be demonstrated in the serum of the horse, rabbit, rat, dog, or of normal human subjects, nor in that of patients with leukaemia or myeloma. Reactions with guinea-pig serum were also demonstrated with tissues taken from mice of C3H strain with plasma-cell tumour and from the same strain with mammary carcinoma, but no positive reactions could be demonstrated with tissues from mice of the white Swiss strain, in sarcoma in C57B mice, in DBA mammary carcinoma, and Walker carcinoma in Lewis-strain rats. The two examples of 6C3.HED Garner lymphoma so far tested failed to show positive agglutination reactions, but did give low-titre precipitin reactions. The tissues of normal animals in all cases gave negative test results.

Various absorption studies were then carried out, these showing that there was a fair amount of cross agglutination. There appeared to be a group antigen as well as a specific antigen for each type of tumour. An interesting point was that tissues from the brain and spinal cord gave positive reactions of the same order of magnitude as cells of bone and bone marrow, even though these tumours rarely show significant leukaemic infiltration. In the authors' opinion this does not appear to be associated with the presence of serum in the tissues examined, and they suggest that AKR leukaemia is a disease of the reticulo-endothelial system in the broadest sense, and that the mesenchymal cells in the brain, although showing no morphological change, undergo some transformation that is detectable by immunological methods. It was not possible, however, in the present series of experiments to determine whether the guinea-pig serum factor is the same as Kidd's protective factor.

The leucocytes in both human and animal leukaemia have been shown to be agglutinated by normal adult guinea-pig serum in tests carried out in test tubes. Slide tests used by some workers have not given positive results, and in the second part of their paper the authors describe an investigation carried out by the slide technique in order to determine the factors affecting leucocytic agglutination. It was found that a certain optimum concentration of cells was necessary, this being between 5,000 and 10,000 cells per c.mm.; concentrations greater or less than this were found to give false negative results. It was shown that an antigen was present in fresh serum (both normal and leukaemic) which can neutralize the agglutination factor present in guinea-pig serum. The optimum temperature appears to be 37° C. and agglutination rarely takes place within the first 15 minutes, but is usually well developed at one hour. On a basis of these investigations a modified slide technique was evolved in which the leucocytes were washed three times in saline to remove all fresh serum; then with an optimum concentration of cells the slide was incubated at 37° C. for one hour and examined microscopically; suitable controls were arranged. With this technique it was possible to obtain a weak positive result by the slide test with cells from 10 patients with leukaemia. The authors conclude that although positive results can be obtained by this means, the test-tube technique is far superior. *R. F. Jennison*

314. Serologic Investigations of Herpes Simplex Virus Infections

H. E. DASCOMB, C. V. ADAIR, and N. ROGERS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **46**, 1–11, July, 1955. 28 refs.

A complement-fixation (C.F.) test for the laboratory diagnosis of herpes simplex is described and the distribution of complement-fixing antibodies in normal population groups is discussed. The test, full details of which are given, is said to provide a simple and rapid procedure for serological investigation of this disease which may supplement or in some cases replace the more laborious neutralization test hitherto employed.

To determine the specificity of the C.F. test for herpes simplex, sera from 52 cases of acute and convalescent non-herpetic disease and from 3 cases of syphilis were tested for C.F. antibody. In none of these was there a diagnostic (fourfold or greater) increase in the amount of the antibody during the course of the illness. Sera obtained from 211 military personnel or their dependents during an illness of presumably non-herpetic aetiology were tested to obtain information on the age distribution of C.F. antibody. In each age group C.F. and neutralizing antibodies were present, the proportion of sera with C.F. antibody being greater in the older than in the younger age groups. There was a very high correlation between the results obtained with the C.F. and neutralization tests.

In 20 patients with primary herpetic disease there was a fourfold or greater increase in C.F. or neutralizing antibody titre during the course of the disease. The titres of both antibodies increased in cases characterized by fever with mucocutaneous lesions and lymphadenopathy or with central nervous system involvement. In afebrile cases, however, no C.F. antibodies developed at any time, though neutralizing antibodies could be demonstrated in some instances. The authors consider that the C.F. test is a reliable diagnostic procedure in cases in which there is sufficient systemic involvement to result in fever, but is of no value in mild, afebrile cases. Sera from 14 patients with recurrent herpetic disease were examined. The results showed that both C.F. and neutralizing antibodies were usually present in the earliest available sample of serum, but in a fair proportion of patients only one or the other antibody increased in titre during convalescence. *R. B. Lucas*

315. Preparation of Poliomyelitis Virus for Production of Vaccine for the 1954 Field Trial

L. N. FARRELL, W. WOOD, H. G. MACMORINE, F. T. SHIMADA, and D. G. GRAHAM. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **46**, 265–272, July, 1955. 2 figs., 11 refs.

For the purposes of the field trial of immunization against poliomyelitis carried out in 1954 in the U.S.A., the Connaught Medical Research Laboratories of the University of Toronto produced altogether 3,280 litres of fluid, derived from tissue cultures of the renal epithelium of monkeys, containing all three types of poliomyelitis virus in a titre of 10^{-6} to 10^{-5}. This was supplied at a rate rising from 93 litres to 320 litres a week to certain U.S. pharmaceutical firms for conversion into vaccine by Salk's technique, most of the vaccine used in the trial originating from this source. The materials and techniques employed in this large-scale cultivation of poliomyelitis virus are described in the present paper, which is chiefly interesting for the over-all data it provides and for its description of the precautions taken to prevent contamination with infectious material derived from the monkeys.

A total of 7,055 monkeys were received in weekly batches of 280; of these, 28 were found to have tuberculosis on the evidence of the tuberculin test or necropsy findings, other disease requiring animals' rejection was found at necropsy in 37, while the kidneys of a further 416 animals, when split longitudinally, showed macroscopic abnormalities, usually due to adrenal rests, and were rejected. Fragments of kidney tissue from the first 420 monkeys used were cultured for *Mycobacterium tuberculosis* with negative results, after which this procedure was abandoned. Bacteriological or mycological contamination was discovered in 102 (12%) of the 851 pools of virus-containing fluid harvested, involving 601 litres out of 5,521 litres (10·8%). The presence of viruses other than poliomyelitis virus, and presumably of monkey origin, was detected in a further 11 pools (76 litres). In 7 of these it was identified, on the basis of rabbit inoculation, as Virus B, which is pathogenic for man; the viruses in the remaining 4 pools await identification. In all, 4,450 litres, or more than 80% of the 5,521 litres of fluid prepared, were of the required standard for virus content and were uncontaminated, allowing the requirements for vaccine preparation to be met with an ample margin. *J. E. M. Whitehead*

316. Some Observations on the Complement-fixation Test for the Psittacosis–Lymphogranuloma Venereum Group of Viruses

D. S. DANE. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 382–384, March 12, 1955. 7 refs.

In describing the method used at the Institute of Medical and Veterinary Science, Adelaide, for the preparation of complement-fixing antigen for the psittacosis-lymphogranuloma group of viruses the author states that he prefers to use the virus of enzootic abortion of ewes to the psittacosis virus, because it is safer to handle and grows to a high titre in the yolk-sac of the hen's egg. The method is described in detail. The virus suspension is placed in a boiling water-bath for 20 minutes, and then after cooling is shaken with ether every few hours for 4 days.

Heating of the antigen suspension and extraction with ether produced an antigen which reacted fully with all "positive" sera, and no reactions occurred in tests on over 600 normal sera and 100 sera from patients suffering from pneumonia and pyrexia of unknown origin. In cases of psittacosis which have been treated with antibiotics complement-fixing antibodies do not always rise to a high level and the reaction may be delayed. Moreover, it is pointed out, a rapid fall in titre may occur during convalescence. For these reasons the serological diagnosis of psittacosis in cases treated with antibiotics is more difficult. *Kate Maunsell*

Pharmacology

317. **Protection against Anaphylactic Shock by Various Substances**
H. HERXHEIMER. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **10**, 160–162, June, 1955. 1 fig., 17 refs.

The author has investigated, at University College Hospital Medical School, London, the anti-anaphylactic action of various substances. Anaphylactic shock was produced in guinea-pigs by the "microshock" method in which the "preconvulsion time", that is, the time elapsing between exposure to an antigenic aerosol and the occurrence of a convulsion is regarded as a measure of the severity of the shock; if the time required to develop shock is significantly prolonged by a drug, this drug is regarded as having a protective effect.

In all, 19 substances were tested; the doses and effects of each are tabulated. The following showed no anti-anaphylactic action at the dose-levels used—ascorbic acid, barium chloride, chloral hydrate, chlorpromazine, cyanocobalamin, dibenzyline, heparin, khellin, phenobarbitone, phenylbutazone, phenylephrine, and salicylic acid. Significant anti-anaphylactic action was shown by methantheline (in a dose of 5 mg. per kg. body weight), propantheline (1 mg. per kg.), "buscopan" (hyoscine N-butyl bromide) (0·1 mg. per kg.), and sodium cyanate (50 mg. per kg.). Other drugs having a significant effect were caffeine (100 mg. per kg.), morphine (50 mg. per kg.), and pethidine (20 mg. per kg.), but, as the author points out, these doses are very high and suggest that the effect is non-specific. *G. B. West*

318. **The Uricosuric Action of Ethyl Biscoumacetate**
R. SOUGIN-MIBASHAN and M. HORWITZ. *Lancet* [*Lancet*] 1, 1191–1197, June 11, 1955. 7 figs., 30 refs.

During the administration of ethyl biscoumacetate to a gouty patient with auricular fibrillation at Groote Schuur Hospital, Cape Town, it was observed that the elevated serum urate level fell to normal. Discontinuance of the drug resulted in a return of the serum urate content to its former high level. Simultaneously less urate was excreted and the ratio of urate to creatinine in the urine decreased. Subsequent experiments showed that ethyl biscoumacetate behaves like a potent uricosuric agent, such as probenicid. There was no clear relationship between either the serum urate level or the urinary output of urate and the daily prothrombin values. Single oral doses of 1·2 or 1·8 g. of biscoumacetate produced an impressive fall, amounting to 46%, in the blood urate level in a normal subject and one of 12% in a gouty patient with severe hypertension and slight renal impairment. In 2 other subjects the earliest clear-cut fall began one to 2 hours after administration, and reached a maximum at 5 hours. The prothrombin time did not lengthen until the next day.

In animal experiments ethyl biscoumacetate and probenicid were given respectively to 2 groups each of 14 rats. The serum and urinary urate levels were determined every hour for 2 hours before and 5 hours after administration of the drug. In each case the urate level in the urine rose and that in the serum fell. In a mongrel dog the injection of probenicid or ethyl biscoumacetate was followed by a significant uricosuric response. In a Dalmatian coach-hound—the only other mammal besides man and the apes to excrete substantial amounts of uric acid in the urine, and in which there is tubular excretion of uric acid in addition to glomerular filtration—the abnormally large urate clearance was reduced by the administration both of probenicid and of ethyl biscoumacetate. In further small-scale investigations of other functions of renal tubular transport the preliminary findings indicated that ethyl biscoumacetate impairs the transport of *para*-aminohippuric acid and phenolsulphonphthalein and may also weakly affect the secretion of penicillin. The relationship of the chemical structure of ethyl biscoumacetate to its uricosuric action and the possible clinical application of the present observations are discussed. *Norval Taylor*

319. **Control of Pulmonary Edema with Silicone Aerosols**
M. NICKERSON and C. F. CURRY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **114**, 138–147, June, 1955. 14 refs.

In experiments carried out at the University of Michigan School of Medicine, Ann Arbor, pulmonary oedema was induced in rabbits by the intravenous injection of 0·1 to 2 mg. of L-adrenaline hydrochloride per kg. body weight. About 2 to 3 minutes after the injection the rabbits showed signs of dyspnoea and cyanosis and began to expel sanguineous, frothy fluid from the mouth and nostrils. At this juncture some of the animals were exposed to an aerosol of a 1-in-10 dilution of an emulsion containing 30% of one of various commercial silicone preparations emulsified with 10% of polyoxyethylene stearate and 4% of glyceryl monostearate, others being left untreated as controls. With a dose of 0·5 mg. of adrenaline per kg. the mortality among the controls was 88%, while doses of 1 mg. and 2 mg. per kg. produced 100% mortality. In the aerosol-treated animals no deaths occurred after 0·5 mg. of adrenaline per kg., and although with higher doses of adrenaline the mortality ranged from 4 to 40%, there was evidence that death at these dose levels was due to the toxic effects of adrenaline and was unrelated to the pulmonary oedema.

In control rats exposed to an atmosphere of 1 part of chlorine per 1,000 for 15 minutes the mortality from pulmonary oedema was 94%, whereas all but 3 of 50 animals similarly exposed to chlorine and then to a silicone aerosol for a period of 30 to 60 minutes were protected. The silicones were less effective in protecting rats exposed to 2 parts of chlorine per thousand, but

again it was probable that death was due to factors other than pulmonary oedema.

Experiments performed on dogs showed that the aerosols did not interfere with oxygen transfer, and their administration to rats over long periods produced no inflammatory or granulomatous changes in the lungs. The two silicone preparations used in the animal experiments (" antifoam clear " and " antifoam A ", both dimethylpolysiloxanes of different viscosities) were the most effective of a wide range of commercial preparations in preventing foaming of 10% serum solution *in vitro* and were selected for that reason. *P. A. Nasmyth*

320. **Antiarrhythmic Action of Ambonestyl**

V. LANZONI and B. B. CLARK. *Circulation Research* [*Circulat. Res.*] **3**, 335–343, July, 1955. 5 figs., 20 refs.

In experiments carried out at Tufts College Medical School, Boston, " ambonestyl " (2-diethylaminoethyl-*iso*nicotinamide), which is closely related to procainamide, was given intravenously to dogs in an effective dosage of approximately 40 mg. per kg. body weight. In 9 animals with tachycardia after coronary ligation the drug reduced heart rate by about one-third with, in 4 animals, conversion to normal sinus rhythm. The electrocardiogram showed, in contrast to the findings with procainamide, that the effect on conduction was insignificant. Ambonestyl caused no change in the diastolic electrical threshold in isolated strips from the right ventricle of the rat, but did increase the refractory period. The drug has no local analgesic, antihistaminic, adrenolytic, or sympatholytic action, and its ganglionic-blocking activity is less than that of procainamide. The effect on blood pressure was slight and variable.

V. J. Woolley

321. **Evaluation of Antacid Liquid Suspensions and Tablets in Relation to Secretory Dynamics**

R. A. LEHMAN and L. POLLACK. *Gastroenterology* [*Gastroenterology*] **29**, 46–55, July, 1955. 7 figs., 7 refs.

The purpose of the investigation described herein was to obtain neutralization curves at *p*H 3 by continuous titration for several antacids in liquid suspension and in tablet form. Commercial preparations containing aluminium hydroxide, magnesium trisilicate, and combinations of aluminium hydroxide and magnesium salts, regarded as representative of the non-systemic, non-alkalinizing class of antacid, were used. In order to suppress peptic activity the dose of antacid must produce 90% neutralization of the acid present or subsequently produced. Liquid suspensions of these antacids reacted rapidly with N/10 hydrochloric acid, so that potential acid protection depended on the dose administered in relation to the rate of acid secretion. Preparations in tablet form with the same nominal antacid potency reacted more slowly, this being ascribed to the slow inherent rate of reaction of a partially dehydrated gel, especially when inadequately subdivided by grinding or chewing. The authors conclude that in the usual dosage antacid tablets frequently fail to neutralize secreted acid as fast as it is formed, with consequent loss of effectiveness. *I. Ansell*

322. **Relative Effectiveness of Anticholinergic Drugs on Basal Gastric Secretion**

D. C. H. SUN, H. SHAY, and J. L. CIMINERA. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 713–718, July 2, 1955. 6 refs.

The effects of ten anticholinergic drugs on the basal gastric secretion of 4 patients with chronic duodenal ulcer were observed and compared at Temple University School of Medicine, Philadelphia, a total of 116 studies being carried out. Two Rehfuss tubes were introduced under fluoroscopic observation, one into the stomach, the other into the metaduodenum, and both were aspirated continuously and simultaneously under a negative pressure of 30 in. (76·2 cm.) H_2O. The stomach was emptied completely and the test begun only after a flow of clear gastric juice and bile in the respective tubes was seen; during the tests the patient maintained the sitting position and was instructed to expectorate all saliva. Specimens of the gastric and duodenal contents were collected for 15-minute periods for one hour before, and for 4 hours after, intraduodenal administration of the drug being tested or of normal saline solution as a control. Aspiration through the gastric tube was discontinued for 10 minutes and through the duodenal tube for 45 minutes following introduction of the drug. Each patient acted as his own control, having previously been the subject of three control studies, each 5 hours in length, on different days with 20 ml. of normal saline; all patients showing periods of anacidity were excluded from the present study. A fourth control study, also lasting for 5 hours, was performed when the evaluation of a series of drugs was completed.

The results showed that the variation in acid output was markedly greater as between different patients than in the same patient from hour to hour and day to day. The criterion for adequate antisecretory potency of the anticholinergic drugs was the production of a *p*H of 4·5 or higher. The dose of each drug was just slightly less than that which produced blurring of vision, palpitation, dizziness, headache, or mental confusion, and in this optimal effective dose propantheline (" probanthine "), long-acting propantheline, mepiperphenidol (" darstine "), methscopolamine bromide (" pamine "), and " elorine " sulphate were effective in inhibiting gastric secretion in all 4 patients. Atropine, methantheline (" banthine ") bromide, and scopolamine N-butylbromide were effective in some of the patients at different times, but G 3012 (diethylaminoethyl dimethylphenyl*cyclo*pentane carboxylate) and homatropine methylbromide were ineffective. The authors state that the optimum effective dose of each drug must be determined by trial for each individual and the drugs cannot be administered in doses based on body weight or a uniform dosage schedule recommended. In older patients, especially males, caution must be exercised in the use of these drugs " to avoid possible undesirable side-effects on urination ". Constipation may occur in some patients under effective doses, but this can be counteracted by simple measures and need not contraindicate use of the method. Because of the small number of patients no general conclusions are drawn (but a larger study, as suitable patients become available, is under way). *Norval Taylor*

Chemotherapy

323. **Studies on the Anti-tumour Activity of *p*-Di-(2-chloroethyl)-aminophenylalanine (Sarcolysine)**
L. F. Larionov, A. S. Khokhlov, E. N. Shkodinskaja, O. S. Vasina, V. I. Troosheikina, and M. A. Novikova. *Lancet* [*Lancet*] **2**, 169–171, July 23, 1955. 3 figs., 12 refs.

The synthesis of DL-*p*-di-(2-chloroethyl)-aminophenylalanine (sarcolysine) and some of its analogues at the Institute of Experimental Pathology and Therapy of Cancer, Moscow, is described. Complete regression of rat sarcoma 45 was achieved by giving 3 or 4 doses of sarcolysine each of 10 mg. per kg. body weight at 72-hour intervals. The sarcolysine was injected intraperitoneally in saline. With other tumours 55 to 80% inhibition of growth was obtained. Large doses of sarcolysine have an inhibitory effect on the haematopoietic system. *G. Calcutt*

324. **Resistance to Antibiotics among the Micro-organisms Isolated in a General Hospital in 1953 and 1954**
A. J. Weil and B. Stempel. *Antibiotic Medicine* [*Antibiot. Med.*] **1**, 319–326, June, 1955. 15 refs.

The incidence of antibiotic-resistant strains among micro-organisms isolated over the period July, 1953, to June, 1954, at the Bronx Hospital, New York, is reported. The results of tests with eight antibiotics on 1,117 bacterial strains isolated in the 12-month period are compared with those obtained in previous surveys at the same hospital. The authors claim that the "trend to increased resistance has come to a halt", but the reason for this is not known. Apparent deviations from this stable state were found to be due to contaminants, not to agents of infection.

Clinical experience in all cases confirmed the results of the tests carried out *in vitro*. At present chloramphenicol appears to be the most effective antibiotic, but this may be due to its restricted use. Of the 1,117 strains, only 17 (1·6%) were not affected by any of the eight antibiotics used. *E. G. Rees*

325. **The Pathology of Trauma Caused by Penicillin in the Central Nervous System.** (Zur Pathologie des Penicillinschadens des Zentralnervensystems)
G. Liebegott. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **115**, 206–225, 1955. 7 figs., bibliography.

In this communication from the City Pathological Institute, Wuppertal, Germany, 4 cases of purpura of the brain following the administration of penicillin are described in detail. The first was that of a man who developed tetanus after cutting his thumb with a piece of rusty metal. The convulsions having been controlled by administration of antitoxin, penicillin was given by intramuscular injection because of a rising temperature. One hour after the seventh injection the patient became restless, there were several more convulsions, and death ensued in a convulsive attack 3 hours later. Necropsy revealed gross cerebral oedema, and histological examination showed that the capillaries of the cerebral hemispheres and the cerebellum were widely dilated and that blood had exuded through the walls of many of them, forming small spherical masses in the centre of which necrosis could be seen. Similar but more severe histological lesions were found in the brain, particularly in the corpus callosum, the pons, and white matter of the cerebellum, of a man suffering from asthma and emphysema who died in coma 8 hours after an intramuscular injection of penicillin.

In the third case, that of a man who was admitted to hospital with emphysema and right-sided cardiac failure as a result of asthma of long standing, penicillin was given on 5 consecutive days. After the fifth injection the patient went into coma and died 36 hours later. In this case also severe oedema of the brain was observed at necropsy and histological examination revealed petechial haemorrhages scattered throughout the brain, but especially in the white matter of the cerebral hemispheres and cerebellum and in the pons and medulla. The last case was that of a woman with lymphatic leukaemia who had been treated with urethane. She developed lobar pneumonia and on admission to hospital was given 3 intravenous injections of penicillin. After the third injection she became unconscious and died 10 hours later. Post mortem much cerebral oedema, with flattening of the convolutions, was found. The histological appearances were similar to those in the other cases, with scattered petechial haemorrhages, but in addition, tiny foci of demyelination were found in the pons and also a diminution in the number of Purkinje cells in the cerebellum.

The author compares the histological picture in these cases with that seen in poisoning with arsphenamine. He considers that in both conditions the lesions seen result from an increased permeability of the capillaries due to an allergic reaction. *Ruby O. Stern*

326. **Oral Administration of Penicillin. A Comparative Study of Benzathine Penicillin, Procaine Penicillin and Potassium Penicillin.** [In English]
S. E. Budolfsen, S. E. Juul Hansen, and E. Rud. *Acta pharmacologica et toxicologica* [*Acta pharmacol. (Kbh.)*] **11**, 49–54, 1955. 1 fig., 9 refs.

A comparative investigation is reported from Marselisborg Hospital, Aarhus, Denmark, of the serum penicillin levels obtained with oral administration of benzathine penicillin, procaine penicillin, and potassium penicillin respectively. Adult bedridden patients, aged 18 to 70 years, were given the three compounds at successive intervals of 24 hours, tablets containing 200,000 units being administered in the morning on an empty stomach

and no food being taken for one hour afterwards. The penicillin concentration was estimated in specimens of undiluted blood serum taken half an hour, one hour, 3 hours and 6 hours after administration, the " agar cup " method with a highly sensitive strain of *Sarcina lutea* being used.

After administration of 600,000 units it was found that potassium penicillin, despite wide individual variations, was absorbed more rapidly and gave a higher maximum concentration and a more prolonged penicillinaemia than either benzathine penicillin or procaine penicillin. The average maximum concentrations were 0·46 unit per ml. for benzathine penicillin (35 patients), 0·74 unit per ml. for procaine penicillin (24 patients), and roughly 2 to 3 units per ml. for potassium penicillin (21 patients). In 83% of the tests with potassium penicillin the concentration at 6 hours was $\geqq$0·03 unit per ml., whereas the same level was observed in only 71% of the 35 tests with benzathine penicillin and in 71% of those with procaine penicillin.

Further tests revealed that the peak concentration of penicillin was, on the average, higher after intramuscular injection of 200,000 units of potassium penicillin than after oral administration of 600,000 units. On the other hand there was a more prolonged penicillinaemia after oral administration. *Norval Taylor*

327. **The Inactivation of Isoniazid by Filtrates and Extracts of Mycobacteria**

A. S. YOUMANS and G. P. YOUMANS. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 196–203, Aug., 1955. 9 refs.

In studies at the Northwestern University Medical School, Chicago, the authors have investigated the relationship between the size of the inoculum of various mycobacteria and the bacteriostatic action of isoniazid, and also the cause of inactivation of this drug. Filtrates of cultures of *Mycobacterium tuberculosis* (Strains H37Rv, H37Ra, and 607), *Myco. phlei*, and one strain of *Escherichia coli* were found to reduce the bacteriostatic action of isoniazid on mycobacteria 2- to 512-fold, the amount of this reduction depending both on the size of the inoculum and on the age of the culture when filtered.

The authors suggest that mycobacteria and perhaps other micro-organisms produce and liberate an " anti-isoniazid " substance. Experiments showed that this substance appears to act rapidly, is non-dialysable, partially inactivated by trypsin, destroyed by *p*H of 2·0, and can be precipitated by ammonium sulphate. The *p*H of the active filtrates ranged from 5·5 (*E. coli*) to 8·8 (*Myco. phlei*). Susceptibility of the substance to heat varied with the source of the filtrate, that produced by Strain 607 of *Myco. tuberculosis* being the most sensitive to heat and that by *Myco. phlei* the most resistant. Sterile aqueous cell extracts, prepared by grinding cultures of Strains 607 and of H37Ra, were more antagonistic to isoniazid than filtrates of these strains, reducing the bacteriostatic activity of the drug 128- to 4,086-fold. This finding suggested that the anti-isoniazid agent may be a soluble intracellular substance which is either excreted into the culture medium during growth or liberated into the medium by autolysis of mycobacterial cells. It was further shown that the H37Rv strain of *Myco. tuberculosis* made resistant *in vitro* to isoniazid produced very little of the anti-isoniazid substance. *Joyce Wright*

328. **Chemotherapy of African Sleeping Sickness. I. Chemotherapy of Experimental *Trypanosoma gambiense* Infection in Mice (*Mus musculus*) with Nitrofurazone**

A. PACKCHANIAN. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 705–711, July, 1955. 7 refs.

Working at the University of Texas School of Medicine, Galveston, the author has investigated the effect of four nitrofuran compounds, in particular nitrofurazone (" furacin "), in the chemotherapy of trypanosomiasis in mice. In these animals intraperitoneal inoculation with 0·2-ml. aliquots of a saline dilution (10 to 20 volumes) of heavily infected heart blood from previously infected mice produced fulminating infections. All untreated mice died within a week, the average duration of the disease being 4 days. Nitrofurazone (5-nitro-2-furaldehyde semicarbazone) was given either orally or intraperitoneally as a suspension in 0·5% aqueous carboxymethyl cellulose, each animal receiving 0·5 ml. per dose. In different groups treatment with the drug was started 24, 48, and 72 hours respectively after inoculation.

In the group given 50 mg. per kg. body weight intraperitoneally the drug exercised a suppressive, but not curative, effect. Three daily doses of 100 mg. per kg. produced a cure rate of 80%. The tail blood of surviving mice was examined periodically and if no trypanosomes were found in the period between 42 and 240 days after infection the animals were presumed to be cured. The results of oral administration of the drug were similar. A suppressive effect was obtained with three daily doses of 25 mg. per kg. body weight, a 40% cure rate with three daily doses of 50 mg. per kg., while four daily doses of 50 mg. per kg. resulted in 90% of the mice being cured when a second course of treatment was given 5 days after the first. Finally, three courses, separated by 5-day intervals, of three daily doses of 50 mg. per kg. body weight resulted in 100% cure in 10 mice.

Of three other nitrofuran compounds tried, 5-nitro-2-furaldehyde thiosemicarbazone intraperitoneally produced complete cure when given in three daily doses of 100 mg. per kg. body weight and was suppressive in two daily doses of 50 mg. per kg.; 5-nitro-2-furfurylidene amino biuret when administered in three daily doses of 50 mg. per kg. exercised a suppressive effect; 5-nitro-2-furaldehyde 2-(2-hydroxyethyl semicarbazone) intraperitoneally in three daily doses of 100 mg. per kg. resulted in the cure of 50% of the animals treated.

The author suggests that nitrofurazone might be tried in cases of African trypanosomiasis in human subjects, a schedule tentatively proposed being 25 mg. per kg. body weight daily for 5 days, followed by a second course after a rest period of 3 to 10 days.

I. M. Rollo

Infectious Diseases

329. **The Bacteriological Diagnosis of Whooping-cough (Due to *Haemophilus pertussis* and *H. parapertussis*) by Aspiration of the Nasopharyngeal Mucus. Preliminary Results.** (Diagnostic bactériologique de la coqueluche (à *Haemophilus pertussis* et à *Haemophilus parapertussis*) par aspiration du mucus nasopharyngien. Premiers résultats)

R. DEBRÉ, J. MARIE, F. HERZOG, H. BOISSIÈRE, and M. GAIFFE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 2203–2207, June 22, 1955. 17 refs.

In this communication from the Centre International de l'Enfance, Paris, the authors claim that by using the technique of aspiration of mucus from the nasopharynx first described by Auger (*J. Pediat.*, 1939, **15**, 641) they have obtained better results in the bacteriological diagnosis of whooping-cough than has been possible by the more usual means. The method, slightly modified, of obtaining the specimen, the simple apparatus, which consists of a syringe, catheter, and rubber tube, and the cultural methods employed are described in detail.

Of 184 cases of whooping-cough *Haemophilus pertussis* was isolated from 95 (51%). These were distributed as follows: 29 positive cultures were obtained in mucus from 35 cases in the catarrhal period, 56 from 84 cases in the first week of coughing, and 10 from 65 cases after the first week of coughing. At the same time 8 positive cultures were obtained in which the organism was identified as *H. parapertussis*.

The authors suggest that these results justify a more prolonged investigation of this method of bacteriological diagnosis. They also point out that the presence in this series of 8 cases of clinical whooping-cough which were apparently due to *H. parapertussis* may explain the occasional occurrence of whooping-cough in immunized subjects, and raises the question whether the routine addition of *H. parapertussis* to the standard pertussis vaccine might increase its prophylactic efficacy.

R. F. Jennison

VIRUS DISEASES

330. **Western Equine and St. Louis Encephalitis. Preliminary Report of a Clinical Follow-up Study in California**

K. H. FINLEY, W. A. LONGSHORE, R. J. PALMER, R. E. COOK, and N. RIGGS. *Neurology* [*Neurology*] **5**, 223–235, April, 1955. 3 figs., 25 refs.

An epidemic of arthropod-borne Western equine and St. Louis encephalitis occurred in central California in 1952, and in this paper from Stanford University, San Francisco, a preliminary follow-up study of psychomotor sequelae of the disease is reported. In view of the short period of follow-up (1½ years) the report is limited to some general observations on the sequelae observed, which included residual upper motor neurone lesions, mental retardation, abnormal behaviour, and mild emotional disturbances. Sequelae were most common in infants infected before the age of 3 months, particularly if convulsions occurred in the acute stage of the disease; recurrence of convulsions was often associated with the most severe psychomotor disturbances. In children who were free from convulsions during the acute stage this complication was unlikely to develop subsequently. Severe sequelae in adults were uncommon, and there was no evidence that Western equine or St. Louis encephalitis caused Parkinsonism. All patients with complications showed a tendency to improve with time.

D. Geraint James

331. **Rubella-encephalitis**

P. SCHLEISNER, J. THORSTEINSSON, and I. BØGESKOV-JENSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **2**, 101–106, July, 1955. 32 refs.

The authors review the 75 cases of encephalitis complicating rubella which have been reported in the literature and describe 4 additional cases observed at Horsens Kommunehospital, Denmark. Three boys and one girl were affected, their ages being 5, 6, 13, and 8 years respectively. In 3 of the cases the patient developed nervous symptoms 2 to 7 days after the rash appeared. These included restlessness, convulsions, coma, hyperreflexia, meningism, and spastic gait. The fourth patient —the 6-year-old boy—developed similar symptoms some weeks after a mild attack of rubella. He also had slight icterus and hyperlipaemia. The cerebrospinal fluid showed a lymphocytic pleocytosis, with an increase in albumin content in 2 cases. Hyperpyrexia developed in 2 cases and was treated successfully with cortisone and chlorpromazine. All 4 patients recovered without residua.

[This is an interesting paper. The diagnosis in the fourth case is doubtful, as the authors themselves admit. The condition being self-limited, it is difficult to assess the value of cortisone and chlorpromazine in its treatment in 2 of these cases.]

I. M. Librach

332. **Encephalitis following Rubella. A Report of Eight Cases**

M. B. JØRGENSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **2**, 106–110, July, 1955. 10 refs.

The author describes 8 cases of encephalitis following rubella which occurred in patients admitted to Blegdams Hospital, Copenhagen, between 1939 and 1955. There were 4 males and 4 females, ranging in age from 7 to 33 years. The interval between the rash and the onset of nervous symptoms was 1 to 6 days (mean 3 days). The symptoms included headache, clouding of consciousness, coma, delirium, periods of motor excitement, convulsions, and meningeal irritation. In 6 cases the temperature rose to 40° C. (104° F.) or more. In all but one case

the cerebrospinal fluid showed a pleocytosis (9 to 100 cells per c.mm.), and in all the protein content was increased. In 2 cases an electroencephalogram obtained at the time of discharge was normal, but in one case in which a tracing was obtained on the 10th day, after the acute symptoms had begun to subside, diffuse dysrhythmia without focal signs was noted.

The illness was mild and short in 4 cases, whereas the other 4 patients were comatose or delirious for periods up to 6 days. Nevertheless there were no deaths, and all the patients were normal on discharge. No follow-up was carried out. Treatment included the prophylactic administration of penicillin, together with sedatives and measures to combat hyperpyrexia and maintain a free airway in comatose patients.

The author concludes with a short review of the symptomatology and clinical course of the condition as reported in the literature, and stresses the importance of taking energetic measures to combat shock, hyperpyrexia, and respiratory embarrassment in the acute stage, since irreversible damage to the brain is rare and those patients who survive the acute attack generally recover completely.

[An excellent paper of the standard one has come to expect from Blegdams Hospital. It should be read in full.] *I. M. Librach*

333. **Poliomyelitis and Tonsillectomy**
MEDICAL RESEARCH COUNCIL COMMITTEE ON INOCULATION PROCEDURES AND NEUROLOGICAL LESIONS. *Lancet* [*Lancet*] **2**, 5–10, July 2, 1955. 12 refs.

In the first part of this paper an analysis is presented of 103 confirmed cases of poliomyelitis occurring in the 3-year period 1951–3 in which tonsillectomy had been performed in the 3 months before onset of the disease. In this group of 103 patients there were 13 with non-paralytic poliomyelitis, 34 with spinal paralysis, 29 with mixed bulbar and spinal involvement, and 27 with bulbar paralysis only. Of the 61 patients who developed poliomyelitis within 3 weeks of tonsillectomy, 44 had bulbar involvement. The large number of patients exhibiting signs of bulbar paralysis shortly after tonsillectomy cannot be explained in terms of age, sex, or seasonal distribution. The findings in this survey support those of a number of workers in the U.S.A.—namely, that the number of patients with bulbar poliomyelitis less than one month after tonsillectomy is significantly higher than would be expected, but that this did not apply to the spinal form of the disease.

In the second part of the paper an investigation is reported of the part played by activating agents such as physical activity, illness, injections, and surgical operations (including tonsillectomy) in the aetiology of poliomyelitis, with particular attention to tonsillectomy performed at any time before the onset of symptoms. For each of 50 patients aged 5 to 15 years a control of the same age, sex, school, and social environment was chosen. Of the patients, 21 had undergone tonsillectomy, compared with 11 of the controls. In no case was the operation performed within 3 weeks of the onset of poliomyelitis; in most cases it had been carried out one year or more previously. Another survey was carried out in a different town 2 years later, and the findings of the two surveys were pooled. Altogether there were 203 patients aged 5 to 15 years and 203 controls. Among the patients with spinal paralysis only there was a slightly higher incidence of tonsillectomy than among controls; among the patients with bulbar paralysis only there was a significantly higher incidence than in controls; the figures for the bulbar–spinal group appeared to be intermediate. The findings suggested that patients whose tonsils had been removed were more likely to develop the bulbar form of poliomyelitis than those with intact tonsils, even if years had elapsed since the operation. *E. H. Johnson*

334. **Effect of Intermittent Positive-pressure Ventilation on Cardiac Output in Poliomyelitis.** [In English]
B. BERNÉUS and A. CARLSTEN. *Acta medica Scandinavica* [*Acta med. scand.*] **152**, 19–30, July 29, 1955. 5 figs., 28 refs.

While it has been demonstrated that the application of intermittent positive-pressure ventilation (I.P.P.V.) is associated with a reduction in cardiac output in normal subjects and patients with circulatory disturbances, the authors believe this to be the first report of an investigation into its effect in patients with respiratory insufficiency due to poliomyelitis. In 9 such cases studied at the Hospital for Infectious Diseases, Stockholm, arterial blood was obtained from an indwelling catheter in the brachial artery, pulmonary arterial pressure was measured by means of an intracardiac catheter, from which various blood samples were taken for oxygen estimations, and oxygen consumption was measured by attaching a Douglas bag to the tracheotomy tube. Blood gas analyses were carried out by Van Slyke's method, and estimations of cardiac output were made on the Fick principle. Recordings were also made of right atrial, pulmonary arterial, brachial arterial, intratracheal, and intra-oesophageal pressures.

The investigation lasted for 5 to 8 hours in each case. All except 2 of the patients could breath spontaneously for some hours, and observations during I.P.P.V. and spontaneous respiration could thus be made on the same patient. Various types of mechanical respirator were used. Oxygen consumption showed little variation during the period of investigation in individual patients. The arterio-venous oxygen difference tended to rise on changing from spontaneous breathing to I.P.P.V. and to fall on return to spontaneous respiration. The cardiac output was considerably greater during spontaneous respiration; the impression gained was that where positive pressure was maintained for one-half of the respiratory cycle (as with the Gullberg respirator) the effect was greater than when the positive-pressure phase was shorter (one-third of the respiratory cycle). During spontaneous breathing the intra-atrial pressure falls in inspiration and rises again in expiration; with I.P.P.V. it was found to rise during the whole positive-pressure phase, so that the longer this phase, the greater the reduction in the venous pressure gradient and hence in cardiac output. Since intra-atrial pressure depends on

intratracheal pressure it is suggested that the effect of I.P.P.V. on cardiac output would be less if there were a negative pressure in the trachea in expiration; an alternative would be to lower the patient's head so as to increase the venous pressure gradient and to improve the return of blood to the heart, as in the treatment of shock.

D. D. C. Howat

335. **On the Effect of Head-low Position during Intermittent Positive-pressure Ventilation.** [In English]
B. BERNÉUS, T. GORDH, H. LINDERHOLM, G. STRÖM, and H. WERNEMAN. *Acta medica Scandinavica* [*Acta med. scand.*] **152**, 31–38, July 29, 1955. 1 fig., 21 refs.

In view of the findings reported in the previous paper [see Abstract 334] investigations were carried out to determine the effect on the cardiac output of patients with respiratory paralysis of intermittent positive-pressure ventilation applied with the patient lying horizontal and with a head-down tilt of 6 degrees. Of the 6 patients studied, 3 had bulbar poliomyelitis and 3 were undergoing surgical operations under light anaesthesia with controlled respiration. The change from horizontal to head-down position did not influence ventilation in the cases of poliomyelitis, but produced a slight decrease in the surgical cases. The oxygen consumption was little affected by the change, but the arterio-venous oxygen difference was markedly reduced in the former cases, an increase in cardiac output occurring as a result of increased stroke volume which in 2 cases persisted for 10 to 20 minutes after return to the horizontal. In the surgical patients an increase occurred in stroke volume, but little or none in cardiac output. It is suggested that this difference may be accounted for by differences in the volume of blood in the lungs and heart in the two groups, this being reduced in cases of poliomyelitis to below the critical level (15% of the total blood volume) above which any increase due to change in posture ceases to affect cardiac output, although the stroke volume is increased, as in the surgical cases. Below this level the cardiac output increases with the pulmonary blood volume. The persistence of the increased cardiac output which was observed in 2 cases after return to the horizontal may be due to the time taken for redistribution of the blood. It is thus possible that the same beneficial effect on the circulation could be obtained by periodic as by sustained tilting of the patient.

D. D. C. Howat

336. **Relation of the New Respiratory Agents to Acute Respiratory Diseases**
H. S. GINSBERG, E. GOLD, W. S. JORDAN, S. KATZ, G. F. BADGER, and J. H. DINGLE. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **45**, 915–922, July, 1955. 16 refs.

The isolation of new viruses from the upper respiratory tract by tissue-culture techniques has necessitated epidemiological investigations to determine their causal relation, if any, to clinical infections. In the study here reported from Western Reserve University, Cleveland, Ohio, serum and secretions from cases of " acute respiratory disease " (A.R.D.) and non-streptococcal exudative pharyngitis occurring in military personnel, hospital patients, and Cleveland families were examined, as also were lyophilized sera, which had been stored since 1944, from volunteers who had been inoculated with secretions from patients with A.R.D., common cold, and primary atypical pneumonia. [The long-term storing of these sera shows commendable sagacity and has provided valuable information on these war-time epidemics.]

The authors were able to demonstrate that the agent which produced A.R.D. in these human-transmission experiments was identical with, or immunologically closely related to, the RI–67 virus of Hilleman and Werner (*Proc. Soc. exp. Biol.* (*N.Y.*), 1954, **85**, 183; *Abstracts of World Medicine*, 1954, **16**, 96), as susceptibility to infection with this agent was correlated directly with the absence of specific neutralizing antibodies and, conversely, some resistance to infection was evident in volunteers whose blood contained specific antibodies at the time of artificial infection. The further investigation of these lyophilized sera also indicated that inoculation with the RI-67 agent did not induce either the cold-haemagglutinin type of atypical pneumonia or the common cold.

This same group of viruses was also found to be responsible for naturally-occurring sporadic cases and epidemic outbreaks of A.R.D. in military personnel and of non-bacterial pharyngitis in Cleveland children.

D. Geraint James

337. **On the Aetiology of Virus Gastroenteritis.** (К этиологии вирусного гастроэнтерита)
V. M. ZHDANOV, V. I. GAVRILOV, and H. P. MUZHENKOVA. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 78–85, No. 6, June, 1955. 2 figs.

In 1953 a sharp outbreak of gastroenteritis occurred among children in a district of one of the Baltic States, individual attacks lasting 3 to 7 days. No bacterial or toxic cause could be found, and the possibility of viral origin was investigated. For this purpose 14 samples of nasopharyngeal washings and 4 of faeces, each sample being derived from 3 children, were collected, filtered, frozen, and later injected intraperitoneally and intramuscularly into day-old suckling mice. Two virus strains were isolated in this way from nasopharyngeal and two from faecal samples, the mice showing general signs of illness after 7 to 10 days, with involvement of the central nervous system leading to paralysis, in particular of the hind legs, and dying within 24 hours. On macroscopical and microscopical examination focal necrosis of the liver and a mild meningitis were the most outstanding findings. Titration showed that the liver and muscles of infected mice contained approximately twice as much virus as brain tissue. Only mice up to 4 days old were susceptible to the virus; older mice and rodents of other species could not be infected even with mouse-propagated virus, which, after several passages, produced symptoms in day-old mice in 3 to 4 days. The serum of 8 out of 9 patients convalescent from the disease contained protecting antibodies against one of the virus strains isolated.

K. Zinnemann

Tuberculosis

338. **Irregular Discharge from Tuberculosis Hospitals. A Major Unsolved Problem**
W. C. LEWIS, T. H. LORENZ, and G. CALDEN. *Psychosomatic Medicine* [*Psychosom. Med.*] **17**, 276–290, July–Aug., 1955. 15 refs.

Only about 50% of tuberculous patients in hospital are able to take full advantage of the care and treatment available; the remainder leave hospital prematurely (" irregular discharge "), and the subsequent course of the disease is less favourable than in those discharged in the ordinary way. At the Veterans Administration Hospital, Madison, Wisconsin, the causes of irregular discharge were studied in 100 consecutive patients (Group A), the findings being compared with those in a similar number of patients (Group B) who completed treatment. It was found that there was a significantly higher number of previous irregular discharges in Group A than in Group B. No difference was observed between the two groups in the incidence of neurotic or psychotic illness, and it did not appear that the life circumstances of patients in Group A were any more difficult than those of patients in Group B. Patients in the former group, however, found it less easy to adapt themselves to hospital life and to the threat of tuberculosis, and early discharge appeared to represent a " turning away " reaction. Anxiety consequent on separation from home seemed to be an important factor in patients in Group A, who appeared to have less capacity to form emotional attachments to other people.

The paper contains some valuable comments on the relationship between patients and also between patients and the medical staff, and includes suggestions concerning the exploration of these and the management of the anxious, unstable patient. *Desmond O'Neill*

DIAGNOSIS AND PROPHYLAXIS

339. **A Tuberculin Survey in a Metropolitan District and its Relation to Morbidity and Mortality**
S. SCHWARTZ, H. KONTERWITZ, D. NATHANSON, and H. MAGNUS. *Diseases of the Chest* [*Dis. Chest*] **28**, 21–34, July, 1955. 7 figs., 4 refs.

To eliminate tuberculosis from a community there must be reduction, successively, in mortality, in the number of new cases, and in the number of individuals infected as shown by a falling tuberculin-reactor rate. To assess the situation in the Jamaica Health District of New York all patients admitted to the Chest Clinic in 1949 and 1950 (excluding those known to be suffering from tuberculosis) were subjected to the Mantoux test, and the incidence of new cases and the mortality during the same period were analysed.

The survey indicated that the tuberculin-reactor rate in the first 15 years of life was " not negligible ", was similar in males and females, and was higher in non-white than in white patients. Up to the age of 15 the rate among contacts was consistently higher than that among non-contacts, but after that age there was no apparent difference in this respect between the two groups. There was a fall in the number of patients giving a positive reaction after the age of 65. The incidence was low in patients under the age of 15, although there were more new cases among females than among males. After this age the incidence rose abruptly, that in females reaching a maximum in the age group 15 to 30 years and that in males continuing to rise to the age of 65 and over. In the age group 45 to 65 years the incidence in males was three times that in females.

Up to the age of 15 the number of deaths from tuberculosis was low but after that age it rose; in females the peak (19·1 per 100,000) occurred in the age group 30 to 45, while in males the death rate continued to rise until in the age group 45 to 65 it was more than 4 times that in females. Of all deaths in the period 17·7% were in non-white patients.

It is admitted that a tuberculin survey based on a chest-clinic population is not truly representative; it served to show, however, that in this community measures of prevention and cure should be concentrated on the older male and the non-white groups. *R. Crawford*

340. **Long-term Results of Vaccination with B.C.G. by Scarification Carried Out in 1947–51 on 15,284 Children of School Age.** (Résultats éloignés de 15,284 vaccinations par le B.C.G. en scarifications, effectuées, de 1947 à 1951, chez des enfants d'âge scolaire)
C. GERNEZ-RIEUX, M. GERVOIS, A. TACQUET, and R. LEBEURRE. *Revue d'hygiene et de médecine sociale* [*Rev. Hyg. Méd. soc.*] **3**, 205–227, 1955. 2 figs., 30 refs.

From the Pasteur Institute, Lille, where Calmette and Guérin first produced B.C.G., the authors report an investigation into the results of B.C.G. vaccination by scarification in 15,284 school children whose ages varied from 6 to 14 years. The investigation was carried out in the industrial district around Lille and covered children vaccinated during the period 1947–51. Tuberculin testing of the whole school population showed a fall in the percentage of positive reactors from 77% in 1910 to 29% in 1950. The tuberculin response of the vaccinated children was positive in over 90% of cases and this was maintained during the period of observation, which in some cases extended to 6 years. The authors compared the incidence of tuberculosis in the vaccinated group with that in 2,063 unvaccinated school children who were under observation from 1949 to 1953, and found that both extra-pulmonary and pulmonary disease were less frequent among the former. They conclude that B.C.G. vaccination is harmless and confers a satisfactory degree of protection. *Franz Heimann*

341. **The Effectiveness of Vaccination against Tuberculosis in Adults.** (Эффективность противотуберкулезной вакцинации у взрослых)
G. G. KARAPETIAN. *Проблемы Туберкулеза* [*Probl. Tuberk.*] 9–14, No. 4, July–Aug., 1955. 6 refs.

In patients with a primary tuberculous infection, especially those who have not received B.C.G. vaccination, the author has observed definite signs of dysfunction of the vegetative nervous system during the first 3 to 8 months. He affirms that vaccination with B.C.G. markedly diminishes the susceptibility to tuberculous infection. Of a group of non-vaccinated subjects 90% were infected in the course of 2 years, whereas of a similar group of vaccinated subjects only 11% were infected during the same period. Of the non-vaccinated adults tuberculous lesions were found in 14·7%, but only in 1·6% of the vaccinated, that is, in only one-ninth, this difference being attributed wholly to the immunity produced by B.C.G. In the author's experience primary tuberculous infection in adults starts, in the majority of cases, as multilocular changes in the lungs or as a broncho-adenitis and very rarely as a pleural effusion.
H. W. Swann

342. **Mesenteric Lymphadenitis Caused by B.C.G.** (La lymphadénite mésentérique " bécégique ")
S. A. KOSTITCH-JOKSITCH. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 2213–2216, June 22, 1955 8 figs., 28 refs.

In this paper from the University Paediatric Clinic, Belgrade, the author analyses the pathological findings at necropsy on 118 infants who had received B.C.G. by the oral route; 14 of these infants had died from tuberculosis and all of them had been in contact since birth with a source of tuberculous infection. The other 104 infants died from various causes, a list of which is given. The age of 116 of the infants at necropsy ranged from 9 days to 1½ years, the other 2 being aged 4½ and 12½ years respectively; these last two had received B.C.G. on several occasions by mouth.

Of the 104 infants dying from causes other than tuberculosis, lesions in the mesenteric lymph nodes were found in 42; in none of these cases, however, was there any evidence of tuberculous infection of the intestinal mucosa. Examination of the lymph nodes stained by the Ziehl–Neelsen technique revealed the presence of acid-fast bacilli in 6 cases, accompanied in 5 instances by necrosis. The infants showing caseation in the nodes were all aged between 4 and 6 months, and the author states that enlargement of the nodes was rarely found in infants older than 8 months. He suggests, therefore, that a regression of the lesions in the lymph nodes begins between 6 and 9 months and seldom leaves any trace.

The correlation between the changes in the mesenteric lymph nodes and in the tuberculin allergy of the infant was also investigated. It was found that of 9 infants in whom caseation of a node was found at necropsy, all had reacted strongly to tuberculin, while in those infants showing only a hypertrophic reaction without necrosis, the tuberculin reaction had been feebly positive. On the other hand the patients without nodal changes at necropsy had been, with few exceptions, tuberculin negative; it is therefore considered likely that the development of tuberculin allergy is linked with tissue changes in the lymph nodes. It was not possible to establish any relationship between clinical signs and symptoms and the development of adenitis. However, the case is described of an infant of 2½ years who suffered an attack of acute abdominal pain resembling appendicitis 6 to 8 weeks after revaccination. At operation a condition of tuberculous mesenteric adenitis was found, and confirmed by histological examination and animal inoculation. In view of the increase in the practice of B.C.G. vaccination by the oral route the author considers that this problem of tuberculous mesenteric adenitis is of considerable importance. *R. F. Jennison*

RESPIRATORY TUBERCULOSIS

343. **Studies in the Aetiology of Pulmonary Tuberculosis**
W. T. C. BERRY and F. A. NASH. *Tubercle* [*Tubercle (Lond.)*] **36**, 164–174, June, 1955. 3 figs., 8 refs.

In the first part of this paper an investigation is reported into the relation between the thickness of the subcutaneous fat layer and susceptibility to pulmonary tuberculosis. Measurements of the layer of skin and surface fat visible on normal mass miniature radiographs were found to correlate well with measurements made on the same subjects with fat calipers. Normal radiographs of 51 subjects (36 males and 15 females) in whom active tuberculosis subsequently developed were chosen, for each of which the radiographs (from the same roll of film) of 2 healthy control subjects of the same age and occupation who had not developed tuberculosis were selected for comparison. Measurements of the thickness of the fat layer were taken at three points, and from these a figure was reached which gave an index of " leanness–fatness ". It was found that on average, the subjects, both male and female, who later developed tuberculosis were about 17% less " fat " than the controls; owing to the smaller number of females and the higher average degree of fatness in both patients and controls, however, this difference was statistically significant only in males.

In a second investigation an attempt was made to determine whether the tuberculous patient could be identified by the shape of the chest. From magnified 35-mm. chest radiographs a tracing was made of the outline of the heart and thoracic cage without showing any lung lesions. These tracings for 100 patients of each sex who had, or later developed, pulmonary tuberculosis were paired with tracings of a similar number of normal chests, independent observers selecting from each pair the outline for the tuberculous patient. A " highly significant preponderance " of radiographs for males with tuberculosis were identified. The tracings were then mixed, shuffled, and sorted into three groups: (1) obviously thin and narrow chests and hearts; (2) " average normal " chests; and (3) broad chests. Only one out of every 10 males with tuberculosis was in

Group 3, while a quarter of the total number with this disease were in Group 1. The authors state that this did not wholly account for the greater leanness observed in the chests of those who later developed tuberculosis.

The reasons for this leanness are discussed; it is suggested that there may be biochemical or other differences from normal which are common to all lean men, and that among these there is one which is important in the aetiology of pulmonary tuberculosis.

G. M. Little

344. **A Physiologic and Clinical Study of Failures in Vitamin A Metabolism in Tuberculous Patients**
H. R. GETZ. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **72**, 218–227, Aug., 1955. 1 fig., 9 refs.

In a previous study the author and colleagues (*Amer. Rev. Tuberc.*, 1951, **64**, 381; *Abstracts of World Medicine*, 1952, **11**, 104) demonstrated a relationship between certain nutritional deficiencies and the development of tuberculosis. The present study, which was begun in 1947 at the Charles Cook Hastings Home, Altadena, California, was carried out on 78 newly diagnosed, previously untreated, male patients suffering from moderately advanced pulmonary tuberculosis when admitted to hospital. All were treated by strict bed rest and an adequate diet, no patient receiving chemotherapy, collapse therapy, or surgery for treatment of the tuberculous condition during the investigation. The plasma levels of vitamin-A alcohol, vitamin-A ester, and carotene were determined at 6-weekly intervals. On admission to hospital, 73% of the patients showed a lowered plasma level of vitamin-A alcohol, but the levels of vitamin-A ester and carotene were normal; 98% suffered from night blindness and 97% had Bitôt's spots on the conjunctiva. These findings were taken to indicate a failure of the tissues to release vitamin-A alcohol from the ester combination; conversion of carotene to vitamin A also appeared to be blocked. It has been shown by other investigators that vitamin-A alcohol normally represents 90 to 95% of the total vitamin A in the systemic circulation.

The patients were divided into three groups. Group 1 (37 patients) received the basic diet only; Group 2 (26 patients) received the diet plus a supplement of various amounts of synthetic vitamin A ranging from 150,000 units daily to 160,000 units per week; Group 3 (15 patients) received the basic diet plus a crude concentrate of cod-liver oil containing 150,000 units of natural vitamin A and 7,500 units of vitamin D. After 180 days 54% of Group 1, 68% of Group 2, and 100% of Group 3 showed a normal level of vitamin-A alcohol in the plasma [all results are expressed in percentages]; the response in patients in Group 3 was conspicuously rapid, all of them ran a good clinical course, and all were discharged with inactive disease; in contrast, 15 out of 37 cases in Group 1 and 10 out of 26 cases in Group 2 were classed as "clinical failures" because of advancing or stationary disease, failure of cavities to close, or tuberculous complication. The author suggests that a factor favourable to healing may be present in the crude concentrate of vitamin A from cod-liver oil. [But he does not say what proportion of the "clinical failures" showed a persistently low level of vitamin-A alcohol in the plasma.]

Joseph Parness

345. **Artificial Pneumothorax Treatment Today**
B. ROBERTS and J. P. LYONS. *Tubercle* [*Tubercle* (*Lond.*)] **36**, 187–193, June, 1955. 5 refs.

An investigation is reported of the subsequent history of 394 patients with established artificial pneumothorax who were discharged from the Grosvenor Sanatorium, Ashford, Kent, between 1942 and 1948 inclusive. The follow-up period was at least 5 years in all cases and in one-third it was 10 years.

At 5 years 41 of the patients had died (38 from tuberculosis), a mortality of 10·4%. Empyema occurred in 15 cases within 5 years of discharge, an incidence of 3·8%; 4 of these patients died, but the authors point out that in 8 other cases in which full details of death were not available empyema may have been present. In 257 cases followed up for 8 years the survival rate was 80·9% and in 109 followed up for 10 years it was 72·48%.

Artificial pneumothorax was induced after January, 1946, in 110 cases, some of which had the benefit of chemotherapy; the survival rate in this group over an average follow-up period of 6 years was 95%. Empyema occurred in 2 cases in this group. Of the 109 patients, 92 were well and working 5 to 7 years after discharge, but 28 required further treatment. A relapse was recorded in only one of the 75 cases in which artificial pneumothorax was abandoned "because it had achieved its object", compared with 17 out of 53 in which it was abandoned prematurely.

G. M. Little

346. **The Blood Sedimentation Rate and Fractional Plasma Viscosity in Pulmonary Tuberculosis**
J. HOUSTON and J. S. LAWRENCE. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 119–128, April, 1955. 3 figs., 16 refs.

Ever since the adoption in clinical practice of determination of the erythrocyte sedimentation rate (E.S.R.) as a measure of the extent of tissue damage in disease and the later discovery of serious fallacies associated with its use, attempts have been made to study the plasma proteins by more direct methods. Among the new techniques investigated was that of determining plasma viscosity during fractionation of proteins, a method which appeared to give a more accurate assessment of disease activity than other suggested tests.

In the study here reported from the Crossley Hospital, Frodsham, Cheshire, the authors determined the E.S.R. and the total and fractional viscosities of the plasma and compared the results with those of a clinical and radiological assessment in 100 consecutive patients with pulmonary tuberculosis, a total of 250 samples of blood being taken at different stages of the disease process. Of these, 50 each were taken (1) during the active, febrile stage of the disease (temperature above 99° F. (37·2° C.)), (2) during the active but afebrile stage, (3) when activity was doubtful, (4) when the disease was probably inactive, and (5) when it was definitely inactive.

Plasma viscosity was determined by the method described by Lawrence (*J. clin. Path.*, 1950, **3**, 332; *Abstracts of World Medicine*, 1951, **9**, 599), and E.S.R. by the Westergren method, except that the estimation was carried out at 37° C. and read after 30 minutes, thus avoiding errors due to variation in room temperature or presence of cold agglutinins.

In all tests a higher proportion of abnormal values was found in the active febrile than in the active afebrile patients. The E.S.R. was raised in only 36% of the clinically active cases, the plasma fibrinogen level in 50%, the total plasma viscosity in 63%, and the γ-globulin viscosity in 68%; the remaining protein fractions proved less helpful. The total and fractional plasma viscosities taken together showed an abnormality in 82% of samples, but the addition of the E.S.R. result added only a further 1%. The extent of the pulmonary disease as determined radiologically influenced the plasma proteins in the same way, the γ globulin showing most response and the E.S.R. being but little affected, while radiological improvement was reflected in the plasma proteins and E.S.R. in the same way as the clinical assessment.

The authors therefore suggest that determination of plasma viscosity gives a useful indication of the activity of the disease in cases of pulmonary tuberculosis, especially if the fractional technique is used, whereas the E.S.R. appears to be of little assistance and a strong case is made for dispensing with it altogether.

P. I. Reed

347. **Combined Intermittent Treatment of Pulmonary Tuberculosis with Three Drugs.** (" Schaukel-Therapie " der Lungentuberkulose mit Dreier-Kombination)
H. BERG and S. SCHRÖDTER. *Tuberkulosearzt* [*Tuberkulosearzt*] **9**, 385–393, July, 1955. 4 figs., 16 refs.

The authors describe their experience at the University Medical Clinic, Rostock, Mecklenburg, of combined, intermittent, alternating treatment with streptomycin, PAS, and isoniazid in the management of 161 cases of pulmonary tuberculosis, and compare the results with those achieved with isoniazid and PAS alone.

The treatment schedule employed was as follows. (1) Isoniazid was given for 14 days, beginning with 100 mg. daily and gradually increasing to 400 mg., the average dosage being about 5 mg. per kg. body weight. (2) After the 14th day PAS was added, a dose of 10 to 12 g. daily being given on 2 days out of every 3. (3) After 4 weeks isoniazid was discontinued, and on the PAS-free days 1 g. of streptomycin intramuscularly was substituted, this regimen being continued for another 4 weeks. (4) After this period the streptomycin was again replaced by isoniazid and the cycle repeated. The total amount of streptomycin given in any course did not exceed 30 g. and the whole course took 9 months to complete.

The 161 patients were divided into three groups showing respectively: (1) fresh exudative lesions with or without cavitation; (2) reactivation of previously stable but long-standing disease; and (3) chronic cavernous lesions. Of the 110 cases in Group 1, 63 were treated with isoniazid and PAS alone and 47 received the combined intermittent treatment (triple therapy); of the 51 cases in Group 2, 30 received isoniazid and PAS, and 21 the combined treatment. (As the number of chronic cases admitted to the clinic was small the results in patients in Group 3 are excluded from the discussion.)

Analysis of the results showed that in both Groups 1 and 2 the over-all improvement, as judged by the fall in temperature and erythrocyte sedimentation rate (E.S.R.), gain in weight, and rate of sputum conversion, was better in patients given the combined treatment than in those treated with isoniazid and PAS alone, but not markedly so. Of the patients in Group 2 given the triple therapy 71% showed sputum conversion, as compared with 53% of those treated with isoniazid and PAS alone. Among the whole series of 161 cases, 130 became sputum-negative; of the remaining 31 patients, in 20 the organisms present were still sensitive to chemotherapy, while in 11 the tubercle bacilli found in the sputum were resistant to either isoniazid or PAS. No case of streptomycin resistance was encountered among those given the triple therapy.

Radiologically, and particularly in respect of cavity closure, there was significantly greater improvement among patients given the combined treatment than in the others; in both groups radiological improvement was more marked than improvement in other respects, that is, in the non-specific reactions such as temperature, E.S.R., weight gain, and sputum conversion.

In conclusion the authors sum up their experience by expressing the conviction that the cases most suitable for triple therapy are those with fresh exudative lesions with or without cavitation. The great advantage of this combined therapy is that it prevents the development of resistance to streptomycin, and this may be a very valuable asset should surgical intervention later become necessary.

[This is a useful paper, but the triple regimen recommended seems somewhat ponderous and could probably be improved upon.] *I. M. Librach*

348. **Tuberculous Disease in Resected Specimens**
P. L. LOGAN. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **71**, 830–840, June, 1955. 7 figs., 15 refs.

At Poole Hospital, Nunthorpe, Yorks, an attempt was made to correlate radiological and macroscopical appearances of resected portions of lung in 43 cases of pulmonary tuberculosis, and to determine how much microscopically demonstrable disease was present in parts of resected specimens which were judged to be normal on *x*-ray and macroscopical examination.

If caseous foci were less than 0·5 cm. in diameter and were not calcified they were generally not visible on the radiograph. Macroscopic disease was often undetected on *x*-ray examination because of breast shadows, mediastinal deviation, and thickening of the basal pleura. Almost every block of tissue from areas of lung judged to be normal showed histological evidence of tuberculosis. In less than half the cases the disease was healed and in one-quarter it was active, although there was no clinical evidence of activity. *E. G. Rees*

Venereal Diseases

349. **Histopathological Studies of Pinta, Yaws, and Syphilis.** (Studien über die Histopathologie von Pinta, Frambösie und Syphilis)
C. M. HASSELMANN. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **201**, 1–8, 1955. 8 figs., 21 refs.

Comparison of the pathological changes associated with the three treponematoses, pinta, yaws (framboesia), and syphilis, shows important differences between them. Thus in the primary lesion of pinta no proliferation of the intima or media of the small vessels occurs such as is seen in syphilis. In the later stages of pinta and yaws the vessels are still unaffected or show only minimal swelling of the endothelium. Another fundamental difference exists between pinta and yaws on the one hand and syphilis on the other in that the " primary " lesion in the former is both clinically and histologically identical with the subsequent generalized lesions. The lesions of pinta show no superficial erosions, unlike those of yaws and syphilis, and do not become necrotic, as is often the case in syphilis and rather less commonly in yaws. *G. W. Csonka*

350. **Studies of the *Treponema pallidum* Immobilization (T.P.I.) Test of Nelson and Mayer in Human Syphilis. I. Clinical Aspects.** (Risultati ed osservazioni sul test di immobilizzazione del treponema pallidum secondo Nelson e Mayer (T.P.I. test) nella sifilide umana. Nota I^a: Il T.P.I. test nei confronti della clinica)
A. G. BELLONE and M. BONELLI. *Giornale italiano di dermatologia e sifilologia* [*G. ital. Derm. Sif.*] **96**, 359–371, July–Aug., 1955. 2 figs., 23 refs.

In performing the treponemal immobilization (T.P.I.) test on 529 samples of serum at the University Dermatological Clinic, Milan, the authors followed on the whole the technique used at the State Serum Institute, Copenhagen, with certain slight modifications which are described. They stress the usefulness of reading the result of the test twice, at 18 and at 42 hours, since they found that at the later time 5% of previously negative results became positive. They also stress the importance of obtaining an inoculum in the very early stage of acute orchitis of the rabbit, as delay at this stage may allow sensitization of the treponemes to occur. In order to save time, equilibration of the basal medium in an atmosphere of nitrogen and carbon dioxide and the extraction of the rabbit testes were both reduced to one hour without ill effect. A further saving of time was effected by the simultaneous preparation of two tests in parallel, but keeping the antigens strictly separated. (A photograph shows the lay-out of apparatus facilitating this modification.) All sera for the T.P.I. test were treated with penicillinase, and for purposes of comparison two flocculation reactions and two complement-fixation tests, in both of which cardiolipin and treponemal (Reiter's) antigen were used, were carried out in parallel.

The results are presented in a table and discussed from the clinical point of view. In sera from 50 non-syphilitic subjects the T.P.I. test was negative in 100%. In sera giving a doubtful result with standard tests the T.P.I. test gave a clear-cut result. The authors point out, however, that a doubtful T.P.I. reaction may occur in cases of primary atypical pneumonia, infectious mononucleosis, leprosy, and malaria, and also if the patient is pregnant. In patients with a primary chancre the T.P.I. reaction is often negative, the " immobilisin " not yet having appeared; in this series in only 16% of cases with a history not exceeding one year since the cure of a primary sore was the reaction positive. The T.P.I. reaction was positive in 61% of cases of cured congenital syphilis, and in 71% of cured secondary syphilis of long standing; in the latter group the classic tests gave an intensely positive result in 15% and a partially positive result in 18%. Again, while 94·9% of long-standing cases of accidentally discovered and of " cured " cardiovascular neurosyphilis gave a positive T.P.I. test result, the standard tests gave 45% strongly positive and 45% weakly positive results.

The authors conclude that the T.P.I. test is the most specific test for syphilis yet available, although it is often negative in cases of primary syphilis and is unnecessary in those giving a strongly positive reaction in the classic serological tests. The main indication for its use therefore lies in the testing of serum giving a weakly positive result in standard tests, especially in cases in which an accurate clinical history is lacking. *F. Hillman*

351. **The Cardiolipin Microflocculation Test in the Serological Diagnosis of Syphilis.** (Der Cardiolipin-Mikroflockungstest in der Serodiagnostic der Syphilis)
H. SCHMIDT. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. I. Abt. Originale* [*Zbl. Bakt., I. Abt. Orig.*] **163**, 258–266, July, 1955. 1 fig., 13 refs.

The author has compared the sensitivity of the cardiolipin microflocculation test (C.M.T.) with that of the Wassermann, Meinicke II, citochol (Sachs–Georgi), and Kolmer cardiolipin complement-fixation tests in the examination of 330 samples of serum, mostly from treated syphilitic patients (but also some non-syphilitic) at the Max Planck Institute, Munich. In 94·2% the C.M.T. result was positive (including 16·3% doubtfully positive) and in 5·8% negative. Positive results with the other tests, in the order given above, were obtained in 38·5%, 82·4%, 85·5%, and 26·4% respectively. The author concludes, therefore, that the C.M.T. is much more sensitive than any of the other serological tests employed, but that the number of doubtful reactions was also significantly higher. Owing to lack of clinical

material a comparison of the test with the classic reactions in early infective syphilis was not possible.

The specificity of the test was studied by examining 41 sera from patients who were clinically non-syphilitic and also 3,000 sera obtained from the immigration authorities, although no clinical details were available for these patients. In the latter group 1·3% of non-specific reactions were obtained, this being attributed in many cases to recent vaccination or inoculation.

Brief details of the technique of the cardiolipin micro-flocculation test are given [which differ in no significant way from those of the well-known V.D.R.L. test].

[This paper, like so many published in Europe recently, suffers from an almost complete lack of clinical data. The publication of the results of a large number of serological tests entirely divorced from clinical findings is a relatively worthless endeavour and contributes very little that is new to the increasingly complicated subject of serology.] *R. D. Catterall*

352. **Do Serum Flocculation Tests Suffice as an Indication of Gonococcal Liver Damage?** (Genügen Serumlabilitätsproben als Beweis für eine gonorrhoische Leberschädigung?)
W. STRUM. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph. (Berl.)*] **199**, 564–577, 1955. 4 figs., 11 refs.

In 405 patients of both sexes, of whom 252 had acute or chronic gonorrhoea (in some cases with complications) and 153 had non-specific infections of the genital tract, liver function tests were performed before the beginning of treatment; in the patients with gonorrhoea the tests were repeated after completion of treatment, but not in the other cases. The eight liver function tests employed were all flocculation reactions; in addition the serum bilirubin content and the erythrocyte sedimentation rate were determined and the urine examined for bile pigments.

In 77 out of the 252 patients with gonococcal infections no evidence of liver dysfunction was found. In the remaining 175 (69·4%) an abnormal result was obtained in one or more of the battery of tests. After treatment, which was usually with penicillin alone, 172 of the patients (68·2%) still showed some abnormal liver function in one or more of the tests; the tests were performed in most cases 8 to 10 days after treatment. In 7·6% of the patients the results of more than 4 tests were abnormal before treatment, and after treatment the proportion was 8·7%.

In the group of patients with non-specific genital infections the results of one or more tests were abnormal in 75·8%, and those of more than four tests in 12·4%, all the tests being performed before treatment was given. In a small number of patients the electrophoretic pattern of the plasma proteins was investigated [but unfortunately no details of the technique used are given]. The author states that this is only a preliminary communication.

[The generally acknowledged difficulty in interpreting liver function tests, especially in the absence of definite clinical indications, and the non-specific nature of serum flocculation tests, together with the lack of detail as to the techniques used in this work, make it very difficult to evaluate this paper.] *R. D. Catterall*

353. **Gonococcus Antigen Possessing Excessive Anticomplementary Activity.** [In English]
L. O. BORGEN. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **37**, 14–17, 1955. 3 refs.

Gonococcal antigen for use in complement-fixation tests is prepared at Ullevål Hospital, Oslo, by growing three strains of gonococci on 30% ascitic-fluid–agar with 1% glucose and 0·1% cystine (or cysteine hydrochloride). The growth is harvested after 24 hours' incubation, washed, and dried *in vacuo* over calcium chloride in volumes of 0·1 to 0·3 ml. Samples are titrated for their anticomplementary and antigenic activity and for non-specific complement fixation with negative sera. If an antigen so prepared is strongly anticomplementary it can be made suitable for use by treatment with alcohol. The contents of one ampoule of the dried preparation are re-suspended in 0·1 ml. of distilled water, 3 ml. of 96% ethanol added, and the mixture incubated at 37° C. for 48 hours, being shaken daily. After adding 6 ml. of distilled water the mixture is heated at 56° C. for 30 minutes and centrifuged at 2,000 r.p.m. for 30 minutes. The deposit is discarded and the supernatant used as antigen. It can be stored at 4° C. and is sufficiently sensitive to be used at a dilution of 1 : 3 or 1 : 4 in saline.

Of 10,540 sera which were tested with an antigen prepared in this way from one which was originally strongly anticomplementary, 166 gave positive reactions. In 70 of these cases the patient had clinical evidence of gonorrhoea and in 86 gonorrhoea was suspected. In the remaining 10 cases the results were thought to be non-specific, there being no history or clinical evidence of gonococcal infection. *A. E. Wilkinson*

354. **Paper Chromatographic Investigations of Two Gonococcic Antigen Preparations, the One Alcohol-containing, the Other Aqueous.** [In English]
O. G. CLAUSEN. *Acta pathologica et microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **37**, 18–20, 1955. 2 refs.

This article from the University Pharmaceutical Institute, Oslo, is published as an addendum to the previous paper [Abstract 353] and describes the results of examination of the anticomplementary suspension of dried gonococci and of the alcoholic extract of the suspension by paper chromatography.

No polysaccharides, simple sugars, or phosphatides could be detected in either antigen, but three nitrogenous substances, which might be lower proteins or amino-acids, were present in both of the extracts. Two of these, of which one was probably cysteine hydrochloride (a constituent of the medium on which the gonococci were grown), were present in considerably greater concentration in the aqueous (anticomplementary) suspension than in the alcoholic extract. The concentration of the other substance appeared to be greater in the alcoholic antigen. *A. E. Wilkinson*

Tropical Medicine

355. **Tropical Eosinophilia Treated with ACTH**
K. S. SANJIVI, K. V. THIRUVENGADAM, and H. C. FRIEDMANN. *Diseases of the Chest* [*Dis. Chest*] **28**, 76–87, July, 1955. 6 figs., 20 refs.

In 24 cases of tropical eosinophilia treated at Madras General Hospital ACTH (corticotrophin) was given intravenously on 10 successive days, 5 units being given on the first day, 10 units on the second, and 20 units daily thereafter until the ninth and tenth days, when the doses were 10 units and 5 units respectively. This regimen produced definite improvement in symptoms, reduced the eosinophilia considerably, increased urinary 17-ketosteroid excretion, and improved the radiographic appearance of the lungs, but the effect was lost very soon after cessation of treatment. These findings are considered to support the view that tropical eosinophilia is a collagen disease or a state of allergy.

R. Crawford

356. **Tropical Eosinophilia Treated with Cortisone**
K. S. SANJIVI, K. V. THIRUVENGADAM, and H. C. FRIEDMANN. *Diseases of the Chest* [*Dis. Chest*] **28**, 88–90, July, 1955. 2 refs.

Cortisone acetate was given by mouth over a period of 10 days in doses rising to 100 mg. on the third day, with gradual reduction on the ninth and tenth days, in 21 cases of tropical eosinophilia treated at Madras General Hospital. Its effects were generally similar to those obtained with ACTH [see Abstract 355]. Although the eosinophil count fell to 400 per c.mm. or less in only 3 of the 21 cases (compared with 15 of 24 cases treated with ACTH), it fell by a mean of 11,997 per c.mm. with cortisone and 14,452 per c.mm. with ACTH, rising again more slowly after treatment with cortisone than with ACTH. The radiographic appearance of the lungs cleared less satisfactorily with cortisone and there was no rise in 17-ketosteroid excretion, but the fall in erythrocyte sedimentation rate was greater and maintained for a longer period than with ACTH.

R. Crawford

357. **The Diagnosis of Amoebic Colitis**
J. A. L. DAVIES. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 491–496, July, 1955. 8 figs., 9 refs.

The diagnosis of chronic amoebiasis is often difficult because amoebae or cysts of *Entamoeba histolytica* may be found in the faeces only after examination of several specimens, and lesions, if present, may be limited to the wall of the caecum or ascending colon and therefore not detectable by sigmoidoscopy. While studying this type of case at the West London Hospital, the author observed localized radiological changes in the caecum and colon after a barium enema. Typically the shadow of the caecum, ascending colon, and occasionally of the sigmoid colon had a shaggy, irregular outline. A cone-shaped deformity of the lower pole of the caecum was also seen in some cases. These abnormalities were found not only in proven cases of amoebiasis but also in those in which *E. histolytica* could not be detected microscopically. After a course of anti-amoebic drugs —"milibis" (bismuth glycollylarsanilate) alone or together with oxytetracycline, or emetine bismuth iodide and chiniofon—the shaggy outline of the bowel disappeared, although the cone-shaped deformity remained. Four cases are described in detail.

The author discusses the differential diagnosis by radiology of amoebic from non-amoebic colitis.

R. A. Neal

358. **Erythromycin Stearate against Systemic Amebiasis in Colombia**
H. H. ANDERSON, T. L. NELSON, C. CARBONO, and J. DIAZ. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 693–698, July, 1955. 7 refs.

Clinical and laboratory evidence of hepatic involvement, including dysfunction of the liver, was found in 45 out of 60 patients with systemic amoebiasis from the Sevilla area of Colombia, these 45 being selected for a trial of the efficacy of erythromycin stearate and fumagillin in the treatment of the disease. Of the tests of liver function employed, the most reliable was the cephalin–cholesterol flocculation test; the icterus index was helpful in the detection of non-amoebic hepatitis. The 45 patients were divided into three groups and treated for 10 to 14 days as follows: (1) 15 received erythromycin in a dosage of 15 mg. per kg. body weight a day; (2) 19 received the same dosage of erythromycin with 0·5 mg. of fumagillin per kg. a day; and (3) 11 received fumagillin only in a dosage of 0·5 mg. per kg. daily for 10 to 14 days. Hepatic amoebiasis cleared up in 14 of the patients in Group 1, 14 of those in Group 2, and 8 in Group 3. Moreover, *Entamoeba histolytica*, demonstrable in the faeces in 35 cases before treatment began, was completely eradicated.

Generally, toxic reactions were mild and included nausea, vomiting, diarrhoea, and abdominal cramps; in only 2 cases were the toxic effects severe enough to necessitate cessation of treatment. *R. A. Neal*

359. **Treatment of Amebiasis with Erythromycin**
V. M. VILLAREJOS. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **4**, 699–704, July, 1955. 8 refs.

Erythromycin, which has been found to possess amoebicidal activity *in vitro*, was tried in 70 cases of chronic and 28 cases of acute amoebiasis in La Paz, Bolivia. The diagnosis was confirmed by the finding of *Entamoeba histolytica* cysts in the faeces in chronic

amoebiasis and amoebae in the faeces in the acute form of the disease. Since erythromycin is largely destroyed by the acid gastric juice it was given in tablets with an acid-resistant coating. A high initial dose of 800 mg. in all cases was followed by 200 mg. every 8 hours to a total of 3·6 g., or 200 mg. every 6 hours to a total of 4·6 g., or 300 mg. every 6 hours to a total of 6·5 g. After treatment the faeces were examined at frequent intervals up to about 3 months.

E. histolytica rapidly disappeared from the faeces in 6% of the cases of chronic amoebiasis but after about 3 months there was a relapse in 8. The best results were obtained in the 36 patients given a total dose of 6·5 g., all of whom were free from *E. histolytica* at the end of treatment; one relapse occurred in this group after 3½ months.

There was rapid clinical improvement in the patients with acute amoebiasis, the number of stools being normal 62 hours after the start of treatment and no amoebae being found after 96 hours. Again the best results were obtained with a total dose of 6·5 g. In one of the 20 patients so treated there was a relapse after 3 months; this patient had previously received erythromycin in inadequate dosage, and the author suggests that the relapse was due to rapid development of drug resistance. [No evidence in support of this hypothesis is provided.] Of 8 patients given 4·6 g. of the drug, 8 had relapsed when examined 2 months after the completion of treatment. No evidence of drug toxicity was observed with these dose levels. *R. A. Neal*

360. **The Activity of Fumagillin in Intestinal Amoebiasis.** (Attività della fumagillina nell'amebiasi intestinale)
G. MENTASTI and L. GRASSTI. *Ospedale maggiore* [*Osped. maggiore*] **43**, 201–205, May, 1955. 10 refs.

At the Ospedale Maggiore, Milan, 25 patients aged 19 to 46 were treated for intestinal amoebiasis with fumagillin in a dosage of 40 to 60 mg. daily for 10 days; 20 of the patients were passing vegetative *Entamoeba histolytica* in their stools and the remainder cysts. In general the patients were asymptomatic at the time of treatment, but 2 were suffering from acute, but not severe, dysentery and 8 complained of previous symptoms probably due to amoebiasis. In 5 of these cases previous treatment with combinations of emetine, acetarsol, and aureomycin had been unsuccessful.

Various side-effects were noted, especially maculopapular rashes and abdominal pain, and nausea and anorexia occurred in 2 cases. In no case, however, was it necessary to interrupt treatment, but the dosage was reduced to 20 mg. a day in one patient who developed a rash, pruritus of the face, chest, and extremities, complete anorexia, and abdominal pain and malaise; for these complications symptomatic treatment, including antihistaminics, proved of value. All the cases appeared to be cured, no amoebae being found in the stools and no relapse occurring during a follow-up period of 8 to 12 months. Fumagillin also appeared to be of value in the treatment of 7 cases of infection with *Trichomonas* and *Giardia*, good results being obtained in 6.
W. H. Horner Andrews

361. **Terramycin in Amebiasis. Comprehensive Laboratory and Clinical Studies Including a Comparative Study with Diodoquin**
Y. ABD EL-GHAFFAR and M. ABD EL-GHAFFAR. *Gastroenterology* [*Gastroenterology*] **29**, 86–95, July, 1955. 26 refs.

At the Abbasiah Faculty of Medicine, Cairo, " terramycin " (oxytetracycline) was tested *in vitro* in a medium of dilute serum plus solidified serum for its action against *Entamoeba histolytica* at 37° C. It was shown that concentrations of 1 in 2,000 destroyed the amoebae, but concentrations of less than 1 in 10,000 stimulated their growth [under the conditions of these experiments]. Indirect evidence was obtained that oxytetracycline acts directly on the amoebae rather than by influencing the concomitant bacteria. It was later shown that the bacteria present in this study were resistant to the antibiotic.

Estimations of the concentration of oxytetracycline in the stools of patients receiving the drug were made. The stool was diluted with 9 parts of water and centrifuged; the supernatant was then passed through a Seitz filter (which removed about 88% of the oxytetracycline) and the concentration of antibiotic remaining in the filtrate was measured by comparing its effect on *Staphylococcus aureus* with that of appropriate dilutions of the drug. After correction for the loss due to filtration it was found that the average concentration on the 8th day of a course of treatment was 360 μg. of the drug per g. of stool after doses of 0·25 g. 6-hourly, 660 μg. after doses of 0·5 g. 6-hourly, and 1,500 μg. after doses of 0·5 g. 4-hourly. Concentration in the stool rose higher the longer administration of the drug was continued. On the basis of their earlier experiments the authors recommend that 0·5 g. of oxytetracycline every 6 hours for 12 days or 0·5 g. every 4 hours for 8 days is the optimum dosage in the treatment of amoebiasis. Lower doses may thereafter be given in continuation of the above schedule, but in the authors' opinion a dosage of 0·25 g. every 6 hours for 4 days should never be employed as this merely serves to produce concentrations which stimulate the amoebae.

During clinical studies oxytetracycline was given to 72 patients with symptomatic, chronic, non-dysenteric, intestinal amoebiasis who were known to have only a few and small ulcers of the intestine. The dose was 0·5 g. every 6 hours for 8 to 10 days. For comparison 58 similar cases were treated with diodoquin in doses of 0·6 g. three times daily for 20 days, together with " sulphathalidine ", 1 g. three times daily for the first 10 days. One week after the end of treatment the stools were negative in all cases, but by the 7th month 43% of the cases treated with oxytetracycline and 32% of those treated with diodoquin had relapsed. However, all the relapses after treatment with diodoquin occurred by the 8th week, whereas those after terramycin were spread out through the whole 7-month period. Oxytetracycline was particularly effective in controlling the immediate acute symptoms, probably because it acted upon the intestinal flora as well as on the amoebae. Oxytetracycline was also given to two patients with liver abscess, but did not produce a cure in either. *F. Hawking*

Allergy

362. **On Histological Reactions in Allergic Nasal Mucosa Caused by Pollen.** [In English]
O. Strömme. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **8**, 251–255, 1955. 11 refs.

The author describes the histological changes observed in the nasal mucosa of guinea-pigs exposed to the pollen or pollen extracts of rye and birch in a series of studies at the City Hospital, Oslo.

The results may be summarized as follows. In normal, non-sensitized animals, particles of pollen or pollen extract are absorbed and pass through the nasal mucosa causing only an insignificant foreign-body reaction, consisting in a slight increase in the number of histiocytes. In the nasal mucosa of sensitized guinea-pigs, however, an immediate reaction to pollen extract occurs, lasting an hour and being accompanied by vasodilatation of the terminal vessels, particularly marked in the glandular layer; in response to solid particulate matter the reaction lasts longer. Leucocytosis appears, but only in the second half-hour is there a massive invasion of eosinophil granulocytes; in the reaction to solid particles the eosinophilic response may last for 24 hours or longer. (It was notable that the eosinophilic invasion stopped abruptly at the boundary between respiratory mucosa and olfactory mucosa.) A typical histological late reaction then appears, reaching a peak by the fourth day. By the fifth day most of the immature lymphoid cells have become plasma cells or small lymphocytes; usually the cellular reaction clears finally by the eighth day. The author suggests that these findings point to the nasal mucosa as an important site of production of antibodies.

A. W. Frankland

363. **The Effect of Corticotropin and Cortisone on Respiratory Function in Bronchial Asthma**
T. W. Fyles, J. A. P. Pare, and B. Rose. *Journal of Allergy* [*J. Allergy*] **26**, 340–358, July, 1955. 10 refs.

At the Royal Victoria Hospital (McGill University), Montreal, the respiratory function of 8 patients with severe and long-standing bronchial asthma was assessed by determining the vital capacity, including residual capacity, degree of intrapulmonary mixing, and maximum breathing capacity. Treatment was then started with corticotrophin, usually with a long-acting preparation of the hormone, and later continued with cortisone, a maintenance dose being established in the usual way; in most cases 100 to 150 mg. per day was found necessary.

All 8 patients improved considerably soon after treatment was begun, in 4 of them all values for pulmonary function, even that for the residual air, returning to normal. In 3 cases a persistently high volume of residual air remained as the only sign of derangement; in one case pulmonary function did not improve in spite of great subjective improvement. It is concluded that the signs of emphysema found in severe chronic asthma are caused by persistent bronchospasm and that they are reversible.

H. Herxheimer

364. **Use of Corticotrophin Gel and Cortisone in Treatment of Severe and Intractable Asthma**
B. M. Davies and D. A. Williams. *British Medical Journal* [*Brit. med. J.*] **2**, 293–296, July 30, 1955. 26 refs.

In the study here reported from the United Cardiff Hospitals the authors used cortisone, corticotrophin, or hydrocortisone in the treatment of 44 patients with severe and intractable asthma and 6 (all male) with chronic bronchitis and bronchospasm (63 courses); 10 patients were treated as out-patients, the remainder being admitted to hospital. All were carefully examined and a history of recent peptic ulceration was considered a contraindication to hormone therapy. The choice between corticotrophin and cortisone was decided mainly on the grounds of availability. Corticotrophin gel (liquefied by standing in warm water) was given intramuscularly with a dry syringe and a 20-gauge needle in a mean dose of 80 units daily for 4 days and 40 units daily for the next 3 days. In some cases it was followed by hydrocortisone tablets. The dosage of cortisone for patients in status asthmaticus was 300 mg., 200 mg., and 100 mg. in divided doses on each of the first 3 days respectively, and then 100 mg. or less per day, usually for 7 to 14 days. In chronic cases the dose was 100 mg. a day for 4 days and 75 mg. a day for 3 days. All patients were given 2 g. of potassium acetate 3 times a day, together with ascorbic acid and a low-sodium diet. In addition, the usual antispasmodics, physiotherapy, and (where necessary) antibiotics were employed.

In the patients with asthma the results were "good" in 49 out of 56 courses (87·5%), "fair" in 3 (5·3%), and "poor" in 3; one patient died. In those with bronchitis the results were good in only 2 of 7 courses, fair in 3, and poor in 3. Complications included one case of severe melaena in a man who had had a duodenal ulcer 16 years previously, 2 cases of severe furunculosis, and one of venous thrombosis and pulmonary infarction in a woman who had spent 6 weeks in bed. Short-lasting oedema, slight hypertension, glycosuria, "moon-face", and euphoria also occurred in a small number of cases. In the patient who died typical widespread bronchial plugging was found at post-mortem examination. After the end of treatment 18 (43%) of the asthmatic patients were free from attacks for over 3 weeks, but late follow-up showed that 19 (46%) should ideally have received more continuous therapy. The authors calculate that these represented only 1 in 80 to 1 in 100 of adult clinic patients. They emphasize the possible danger of suppression of spontaneous adrenal activity by continuous cortisone treatment.

L. Capper

Nutrition and Metabolism

365. **Comparative Studies of the Effect of Massive Intramuscular Doses of Vitamins D_2 and D_3 in Infantile Rickets.** (Vergleichende Untersuchungen über die Wirkung der intramuskularen Stosstherapie mit Vitamin D_2 und D_3 bei der Säuglingsrachitis)
H. KALOUD. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **11**, 216–221, 1955. 2 figs., 7 refs.

Having previously compared the efficacy of vitamin D_3, the naturally occurring form, and vitamin D_2 (calciferol), given orally in single large doses, in the treatment of rachitic infants (*Öst. Z. Kinderheilk.*, 1953, **9**, 66), the author now reports a comparison of the effects of the two vitamins administered intramuscularly to 24 rachitic infants at the University Paediatric Clinic, Graz.

Each infant received one injection of 15 mg. (600,000 i.u.) of the vitamin, 13 receiving vitamin D_3 and 11 vitamin D_2. Vitamin D_3 produced significantly more rapid healing, as shown by improvement in the craniotabes and by an increase in the serum calcium:phosphorus ratio. Thus craniotabes began to heal in an average of 7·2 days with vitamin D_3 and 10·8 days with vitamin D_2, healing being complete in 16 and 23 days respectively. Similarly there was a significant rise in the Ca:P ratio within 2 weeks with vitamin D_3, but none even after 3 weeks with vitamin D_2. Final healing, however, was achieved equally well with both vitamins.
John Yudkin

366. **Effects of Dietary Protein, Lipotropic Factors, and Re-alimentation on Total Hepatic Lipids and Their Distribution**
C. H. BEST, W. S. HARTROFT, C. C. LUCAS, and J. H. RIDOUT. *British Medical Journal* [*Brit. med. J.*] **1**, 1439–1444, June 18, 1955. 8 figs., 33 refs.

In the study of the effect of diet on total hepatic lipids and their distribution here reported from the University of Toronto the livers of rats which had been fed on various diets for periods of 3 weeks were removed immediately after the animals were killed, a small portion being set aside for histological examination and the remainder analysed for total lipids by extraction with hot alcohol and rectification of the residue with 3 : 1 petroleum ether and chloroform.

In animals receiving diets which contained only 3, 6, or 9% of protein but which was supplemented with methionine (a choline precursor), fat was demonstrable mainly in the periportal regions. The presence of choline, even in large amounts, did not entirely prevent the deposition of fat. In animals given a diet from which the supplementary methionine was omitted the bulk of the fat appeared in the centrilobular areas, and the total lipid content of the liver was grossly increased. The addition of choline reduced the total lipid content to within the normal range, although a small amount of fat could still be seen in the centrilobular and periportal areas. The findings were similar whether the diet was continued for 3 weeks or for 3 months.

On diets containing only 3% casein but supplemented with methionine the rats ate poorly and lost weight, and an increasing amount of fat was deposited in the periportal region. However, when the protein content of the diet was raised to 18% the animals ate better and gained weight; there was a dramatic increase in periportal fat during the first few days on this curative diet, but this disappeared again and the liver was normal histologically and chemically at the end of 3 weeks.

Of the various proteins incorporated in the diets, fibrin was more effective than casein in protecting the liver cells, and vegetable protein (soya bean) was the least protective.
Robert de Mowbray

367. **A Complex Endocrine Disorder in the Pathogenesis of Gout.** (Una complessa disfunzione endocrina nella patogenesi della gotta)
M. ZACCO and M. PERRINI. *Reumatismo* [*Reumatismo*] **7**, 138–147, May–June, 1955. 3 figs., 26 refs.

It has been shown by Robinson *et al.* that when the administration of ACTH to gouty individuals is stopped the urinary 17-ketosteroid excretion and fasting blood sugar level show no such "rebound" phenomenon as is seen in healthy persons. The "rebound" phenomenon being an expression of the speed of recovery of pituitary–adrenal function after a period of substitution therapy with ACTH, that function would appear to be depressed in gout. Moreover, Wolfson *et al.* have shown that the retention of uric acid in gout may be due in part to deficient secretion of 11-oxysteroids by the adrenal glands.

At the Medical Clinic of the University of Bari the present authors have therefore studied the urinary 17-ketosteroid excretion of 8 male gouty patients (during an asymptomatic interval) and of 5 healthy male subjects, all between 40 and 60 years of age, by chromatographic methods. Their results confirm Wolfson's finding that the total urinary 17-ketosteroid excretion is diminished in gout, but provide no support for his hypothesis that this is due to the presence of an "abnormal androgen" which cannot be metabolized into 17-ketosteroids. Chromatographic analysis of the urinary 17-ketosteroids showed that although the excretion of all fractions was reduced, the reduction of Fractions IV and V, which are mainly of gonadal origin, was proportionally greater than that of Fractions III and VII (11-oxysteroids), both of which are of adrenal origin.
V. C. Medyei

368. **Myoglobinuria in Man. With Special Reference to a Familial Form.** [In English]
R. HED. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, Suppl. 303, 1–107, 1955. 10 figs., bibliography.

Gastroenterology

369. **Partial Eventration of the Right Diaphragm (Congenital Diaphragmatic Herniation of the Liver)**
A. VOGL and A. SMALL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 61–82, July, 1955. 14 figs., 44 refs.

Six cases of partial eventration of the right diaphragm with herniation of the liver are reported. The frequent occurrence of this anomaly and the importance of its differentiation from other intrathoracic, pericardial, pleural, diaphragmatic and subdiaphragmatic masses are discussed. The characteristic radiologic features are described, and the use of an artificial pneumoperitoneum for final diagnosis is discussed. The latter is not regarded as an indispensable diagnostic measure.

Aplasia of the diaphragmatic muscle in an area derived from the embryonic septum transversum is offered as a possible explanation for the more common type of hernia of the right diaphragm which is known to exist at birth and is found regularly at the same location. The term congenital diaphragmatic herniation of the liver is suggested as most appropriate for the condition.—[Authors' summary.]

370. **Acute and Subacute Terminal Ileitis.** (Les iléites terminales aiguës et subaiguës)
M. CHÉRIGIÉ, C. TAVERNIER, —. DUPAS, and —. RAYNAL. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 2417–2427, July 6, 1955. 24 figs.

The frequency of appendicular symptoms in children with the infectious fevers, particularly measles, led the authors to investigate the radiological appearances of the lymphatic tissue in the terminal ileum. At the Hôpital Claude-Bernard, Paris, 70 young patients [ages not stated] were investigated by barium enema, and in 58 of these it was possible to examine the terminal ileum. Graduated compression was used to demonstrate the mucosal pattern. Normally in children the terminal ileum is 2 to 3 cm. in diameter and compression reveals longitudinal folds of an inconstant nature. It is generally held that lymphoid follicles may frequently be seen in normal children, but this is not the authors' experience; they believe that these are seen only within 1 cm. of the ileocaecal valve, and consider that extensive lymphatic enlargement in the terminal ileum is definitely abnormal. The lymphoid follicles, when enlarged, project into the intestinal lumen, producing a studded appearance, with residues of barium in mucosal furrows surrounding the follicles. The terminal ileum may also be dilated, the Peyer's patches lying along the free border of the intestine and producing localized filling defects. Such defects may also be due to lymph-node enlargement. There is considerable individual variation in the amount and distribution of lymphatic tissue.

The authors state that hypertrophy of this lymphatic tissue commonly accompanies the lymphadenopathy of infectious fevers such as measles, scarlatina, tonsillitis, and pneumonia, and may also occur in the presence of infestation by ascarids. This lymphoid hypertrophy is believed to account for the appendicular symptoms which may precede the rash in infectious fevers. "Primary mesenteric adenitis" is probably a similar condition. Tuberculosis, Crohn's disease, and typhoid fever sometimes also cause a lymphoid hypertrophy in their earlier stages, later going on to ulceration.

[Only 9 normal children were examined and in 3 of these apparently the presence of lymphoid follicles was demonstrated.] *G. Ansell*

STOMACH AND DUODENUM

371. **Peptic Ulcer in General Practice**
D. I. FINER and J. FRY. *British Medical Journal* [*Brit. med. J.*] **2**, 169–172, July 16, 1955. 10 refs.

The incidence, natural course, and results of treatment of peptic ulcer in two adjoining general practices in a residential area in south-east London, with a population at risk of about 11,000 patients, are reported. On July 1, 1954, there were 177 proven cases of peptic ulcer, the condition having been present for 5 years or more in 124. An attempt is made to determine the extent and degree of disability from peptic ulcer from the number of attendances for consultation concerning symptoms and from the duration of incapacity for work. The results of medical and/or surgical treatment are assessed, attendance figures again being used as indices. The course of the disease was complicated by haemorrhage in 18% of the 124 cases and by perforation in 10%.

Finally, a plea is made for the greater use of the field of general practice as a source of information concerning the natural history of and morbidity from certain common diseases such as peptic ulceration, hypertension, rheumatism, and respiratory infections.
J. Warwick Buckler

372. **Gastro-intestinal Ulceration and Non-ulcerative Dyspepsia in an Urban General Practice**
S. LIPETZ, S. A. SKLAROFF, and L. STEIN. *British Medical Journal* [*Brit. med. J.*] **2**, 172–177, July 16, 1955. 1 fig., 12 refs.

In a general practice in Edinburgh the incidence of peptic ulcer over a 20-year period and the prevalence of this condition at one date in August, 1953, were studied. During the 20-year period 323 cases were diagnosed, 273 of duodenal ulcer and 50 of gastric ulcer. The age at which duodenal ulcer was first diagnosed was most commonly 30 to 44 years for males and 35 to 49 years for females. The incidence of peptic ulcer at August, 1953, was high (4·7% of the patients at risk), particularly in the age group 45 to 59 years; in this

age group one out of every 10 patients had peptic ulcer, the figure for males alone being one out of every 6. The authors discuss the reasons for this and analyse the incidence of haemorrhage, perforation, and relapse. They also attempt an assessment of the prevalence of cases of chronic dyspepsia due to causes other than peptic ulceration, and for this purpose divide the cases into 3 main groups: (1) clinically suggestive of peptic ulcer but not proven; (2) suggestive of biliary or cholecystic dysfunction; (3) non-specific dyspepsia—the largest group. Among males there were more cases of peptic ulcer than of chronic dyspepsia, and among females only slightly fewer cases of ulcer than of dyspepsia. This is attributed by the authors to the "consistent screening procedure and continuing investigation of doubtful cases of dyspepsia".

The value in general practice of the Gregersen slide test for the detection of occult blood in the faeces is emphasized. Finally, the authors draw attention to the unique opportunity afforded in general practice for the long-term investigation of dyspepsia.

J. Warwick Buckler

373. **Acute Perforated Peptic Ulcer. Frequency and Incidence in the West of Scotland**
R. A. JAMIESON. *British Medical Journal* [*Brit. med. J.*] **2**, 222–227, July 23, 1955. 10 figs., 4 refs.

This is a survey of 6,343 cases of perforated peptic ulcer occurring during the 10-year period 1944–53 in a well-defined area in the West of Scotland having a population of about 2,000,000 persons, bringing up to date a previous survey of the same area for the period 1924–43, the results of which have already been published (Illingworth *et al.*, *Brit. med. J.*, 1944, **2**, 617, 655; Jamieson, ibid., 1947, **2**, 289). From the data and graphs provided it is possible to draw certain conclusions as to the incidence and prognosis of perforation.

It is shown that there has been a constant and, apart from 1940–41 when the incidence was exceptionally high, an even rise in the incidence of perforated ulcer during the past 30 years in this area. The incidence varies with age, rising from the 20th to the 40th year, being highest from the 40th to the 50th year, and thereafter decreasing rapidly. The preponderance of incidence in males over that in females has fallen from 19 : 1 in 1924–43 to 12 : 1 for the period 1944–53.

The incidence also varies with the season, day of the week, and hour of the day. Relatively few cases occur between September and November, but there is a steep rise in incidence in December and January. Ulcers perforate most frequently on Fridays and Saturdays, least frequently on Sundays and Mondays. Incidence during the 24 hours of the day shows four peaks, the biggest of which is at 5 p.m.; smaller peaks occur at 12 noon and at 10 p.m., and there is a minor peak at 2 a.m.

During the past 30 years the mortality from perforation has fallen from 25 to 8%. Mortality increases with advancing age and with delay before operation. The prognosis is less favourable for perforation of a gastric than a duodenal ulcer. *Zachary Cope*

374. **ABO Blood-groups and Gastric Acidity**
K. H. KØSTER, E. SINDRUP, and V. SEELE. *Lancet* [*Lancet*] **2**, 52–55, July 9, 1955. 3 figs., 18 refs.

The distribution of ABO blood groups in 413 cases of carcinoma of the stomach, 1,047 consecutive cases of peptic ulcer, and 111 cases of pernicious anaemia was studied at Bispebjerg Hospital, Copenhagen, the distribution of these blood groups in 14,304 healthy subjects aged 15 to 70 years being used for purposes of comparison. Of the patients with carcinoma of the stomach, 51·3% had Group-A blood (controls, 44%). Histamine-fast achlorhydria was present in 195 (out of 301) of these patients, and in this group the incidence of Group-A blood was very high (56·4%) while that of Group-O blood was correspondingly low (33·2%). Of patients with peptic ulcer only 39·3% had Group-A blood (controls 44%), but 48·7% had Group-O blood (controls 40%). No significant difference was observed in the distribution of ABO blood groups between patients with pernicious anaemia and controls.

Further work on the distribution of blood groups in patients with achlorhydria not caused by cancer of the stomach is being carried out. *I. McLean Baird*

375. **The Relationship of the ABO Blood Groups to Duodenal and Gastric Ulceration**
C. A. CLARKE, W. K. COWAN, J. W. EDWARDS, A. W. HOWEL-EVANS, R. B. MCCONNELL, J. C. WOODROW, and P. M. SHEPPARD. *British Medical Journal* [*Brit. med. J.*] **2**, 643–646, Sept. 10, 1955. 5 refs.

The distribution of the ABO blood groups among 1,665 patients with gastric or duodenal ulcer who were treated at 3 Liverpool hospitals between 1948 and 1954 was compared with their distribution among the total of 15,407 patients whose blood group had been determined at the same hospitals during the same period. The use of the second group of patients as controls was justified by the finding that the distribution of blood groups among them was not significantly different from that found at the Nuffield Blood Group Centre among blood donors drawn from the areas served by the 3 hospitals.

Patients with both gastric and duodenal ulcers or in whom the site of the ulcer was uncertain were excluded and the rest were divided into four groups according to the site of the ulcer (duodenum or stomach) and whether the diagnosis was made macroscopically (at necropsy or operation, or on gastroscopy) or radiologically. The results showed that in all 3 hospitals there was a significantly greater frequency of Group O among patients with duodenal ulcer than among the controls and the patients with gastric ulcer, there being no difference in blood-group frequencies between patients with gastric ulcer and the controls. Among the patients with duodenal ulcer a difference was found at one hospital between those in whom the diagnosis was established macroscopically and those in whom it was established radiologically—surprisingly, the greater excess of Group O was found in the latter.

These results accord with those previously reported by Aird *et al.* (*Brit. med. J.*, 1954, **2**, 315; *Abstracts of World*

Medicine, 1954, **16**, 464), except that Aird also found an excess of Group O among patients with gastric ulcer—though less marked than that among patients with duodenal ulcer.

It has been suggested that the ABO genes may in some way modify the amount of acid secreted in the gastric juice or that they may exercise a protective action on the gastro-duodenal mucosa. The latter suggestion is supported by the preliminary results of an investigation into the ABO–secretor status of patients with duodenal ulcer, which indicate that they may contain an abnormally high proportion of non-secretors. *Richard Doll*

376. **Duodenal Ulcer Treated by Vagotomy and Gastro-enterostomy. Results of 100 Consecutive Cases**
G. F. Henson and C. G. Rob. *British Medical Journal* [*Brit. med. J.*] **2**, 588–589, Sept. 3, 1955.

The results obtained with vagotomy and retrocolic gastro-enterostomy in 100 consecutive cases of duodenal ulcer at St. Mary's Hospital, London, are reported. There was one postoperative death and 10 patients were lost to follow-up; the remaining 89 patients were followed up, on the average, for 29 months. In 11 ulceration had recurred, 5 had persistent dyspepsia, and 30 had persistent postoperative disturbances with or without dyspepsia. In 42 the results were classified as " excellent " or " good ". One patient remained well for 22 months after operation and then had severe melaena.

[This report makes dismal reading, and the authors' conclusion that in their hands the operation is unsatisfactory is a just one. Clearly the results do not compare favourably with those of gastric resection.]
Roland N. Jones

377. **Primary Carcinoma of the Duodenum. Report of 15 Cases**
R. L. Brenner and C. H. Brown. *Gastroenterology* [*Gastroenterology*] **29**, 189–198, Aug., 1955. 3 figs., 32 refs.

LIVER

378. **Excretory Function of the Liver. A Re-assessment**
W. H. Horner Andrews. *Lancet* [*Lancet*] **2**, 166–169, July 23, 1955. Bibliography.

In this thoughtful paper the author expounds his quite original views on the excretory function of the liver—that is, on the excretion of bile and particularly of bile pigment. He states that " it has been assumed for centuries " [in fact, however, only since the work of van den Bergh, around 1920] that the parenchymal cells of the liver secrete [in fact, excrete] bile, and that the assumption " appears to have remained unchallenged —and unproven ". This view, as the author indicates, is the basis of modern classifications of jaundice, but he points out various ways in which it is difficult to reconcile it with all the known facts. The chief of these difficulties, known to all interested in hepatic disease, is to account for those cases in which, clinically, there is obstructive jaundice and this diagnosis is confirmed by the usual biochemical tests, and yet on post-mortem examination the biliary tract is found to be entirely open and unobstructed.

The author now advances the hypothesis that the epithelium of the bile ducts, and not the parenchymal cells, secretes most, if not all, of the constituents of the bile. He bases his hypothesis on the following evidence [none of which, in the abstracter's opinion, is very convincing, although all is interesting and worth thinking about]. (1) Embryologically, it seems likely that the bile ducts develop separately, and therefore may be separated functionally, from the parenchyma. (2) The hypothesis, that in those cases already referred to of obstructive jaundice with patent biliary passages the bile-duct epithelium is unduly permeable to the formed bile, which passes through it into the circulation, is unsatisfactory and unproven. (3) Experimental evidence suggests that " bromsulphalein " is abstracted by the liver from blood supplied to it by the hepatic artery to a much greater extent than from that supplied by the portal vein. The author states that " the portal tracts are the only part of the liver which receive a predominantly arterial blood-supply " (the parenchymal supply being mainly from the portal vein) " and it therefore appears probable that bromsulphalein is removed from the blood supplying the bile-duct ". Since there is some evidence that bromsulphalein and bilirubin are excreted by the same mechanism this conclusion may also apply to bilirubin.

[This " re-assessment " of the excretory function of the liver will interest all who are actively engaged on the investigation of hepatic diseases and jaundice.]
J. W. McNee

379. **Vasomotor Disturbances in Hepato-lenticular Degeneration and Other Liver Diseases.** (Сосудодвигательные расстройства при гепато-лентикулярной дегенерации и других болезнях печени (К проблеме патогенеза сосудистой гипотонии))
N. V. Konovalov. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 269–281, 1955. 9 figs., 21 refs.

Vascular disturbances are an important feature in the clinical course of hepato-lenticular degeneration. They manifest themselves in the form of a haemorrhagic syndrome, as in severe general hepatic disease, an atonic condition of the capillary circulation, acute disturbances of an allergic nature (for example, Schönlein–Henoch purpura), or as epistaxis, bleeding gums, and subcutaneous ecchymoses; the last-named are rarely absent. Sometimes these changes precede the development of progressive brain disturbance. They may temporarily disappear, and in such cases their return may be associated with indiscretions of diet leading to digestive disturbances or with gastro-intestinal infections. Very frequently they reappear after a septic infection such as tonsillitis. Barbiturates have an unfavourable influence if taken over long periods.

Investigation of the blood reveals other abnormalities; the number of blood platelets is diminished, the blood content of fibrinogen and prothrombin is low,

and there is a deficiency of vitamins C, P, and K. Progressive night-blindness is a frequent finding. From the clinical aspect the capillary changes are shown by the ruddiness of the face and cyanosis of the buccal mucous membrane and the nail-beds, and also in the spider angiomata of the skin and marbling on the limbs. Moreover, Khondkarian, who has carried out extensive capillaroscopic investigations in such cases, reported the frequent finding of dilated capillaries, often with aneurysmal swelling of the walls, and stasis of the blood stream; contrary to its usual action, adrenaline increases the loss of tone of the capillaries in this condition. Rolle, employing capillaroscopic and oscillometric methods, has demonstrated diminished response in the vasomotor reflexes, both conditioned and unconditioned, to various stimuli (including verbal), the responses being weak or absent and in many cases even inverted—that is, a stimulus which normally provoked constriction is found to evoke vasodilatation, and vice versa.

The author attributes these vasomotor disturbances to circulating toxins acting both locally upon the walls of the vessels and centrally upon the vasomotor centres. In the present state of knowledge he is not prepared to commit himself as to which of these processes is primary, but he regards them both as dependent upon the hepatic insufficiency, and the cerebral lesions as a consequence of the vascular disturbances and resulting stasis. He instances cases of localized necrosis in somatic and cardiac muscle which were obviously due to microscopic vascular lesions. *L. Firman-Edwards*

380. **The Effect of Oral Protein and Glucose Feeding on Splanchnic Blood Flow and Oxygen Utilization in Normal and Cirrhotic Subjects**
J. L. Brandt, L. Castleman, H. D. Ruskin, J. Greenwald, and J. J. Kelly. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1017–1025, July, 1955. 18 refs.

In studies carried out at Kings County Hospital, Brooklyn, New York, the authors, using the hepatic venous catheterization technique, have shown that in normal subjects splanchnic blood flow increased by 23% and splanchnic oxygen consumption by 50% following the ingestion of a meat meal containing 60 g. of protein. In a group of cirrhotic patients the splanchnic oxygen consumption increased, on the average, 31% after a similar amount of protein. It was also shown that the amino-acid content of the blood in the hepatic vein rose higher in cirrhotic patients than in normal subjects after a protein meal. The ingestion of 100 g. of glucose, on the other hand, caused little change in splanchnic blood flow and splanchnic oxygen requirements. During the investigations it was also observed that in icteric cirrhotic subjects the oxygen difference between arterial and hepatic-vein blood was very low, averaging 2·5 ml. per 100 ml. as against 3·9 ml. in normal subjects and 4·9 ml. per 100 ml. in non-icteric cirrhotic patients.

These findings are discussed in relation to the harmful consequences of high-protein diets in patients with hepatic cirrhosis and the possible benefits of a limited protein intake supplemented with glucose to make up the caloric content. *J. McMichael*

PANCREAS

381. **The Use of Radioactive-labeled Proteins and Fat in the Evaluation of Pancreatic Disorders**
W. W. Shingleton, M. H. Wells, G. J. Baylin, J. M. Ruffin, and A. Saunders. *Surgery* [*Surgery*] **38**, 134–142, July, 1955. 7 figs., 2 refs.

The authors describe trials carried out on dogs and human subjects at Duke University School of Medicine, Durham, N. Carolina, of a diagnostic test for chronic pancreatic disease based on the measurement of the ability of the subject to digest and absorb a standard test meal of protein or fat labelled with radioactive iodine (^{131}I).

After saturating the thyroid gland with iodine by giving 30 drops of saturated potassium iodide solution daily for 3 days, the fasting subject was given a standard protein or fat meal. The former consisted of 0·5 g. of gelatin per kg. body weight in 200 ml. of water, to which was added serum albumin labelled with 50 μc. of ^{131}I, while the standard fat meal consisted of an emulsion containing 0·5 ml. of peanut oil per kg. in an equal volume of water, to which was added glycerol trioleate labelled with 50 μc. of ^{131}I. Samples of venous blood were then withdrawn at 15-minute intervals for 3 hours after the protein meal and at 30-minute intervals for 6 hours after the fat meal, their radioactivity measured by a scintillation well counter, and the ^{131}I content of the total blood volume (calculated as 7·2% of body weight) estimated and expressed as a percentage of the ingested dose. In this way an absorption curve could be drawn for each meal, the slope of which was determined by the rate of digestion of the meal and absorption of the ^{131}I thus set free.

Control tests were carried out on healthy dogs with both the protein meal (20 tests on 15 dogs) and the fat meal (15 tests on 11 dogs) and average absorption curves established. The dogs were then subjected to total pancreatectomy and the tests repeated 1 to 2 weeks later. The curves for both protein (10 dogs) and fat meals (11 dogs) showed a marked decrease in the rate of absorption of ^{131}I, the isotope content of the blood rising more slowly after the fat than after the protein meal. The test was also carried out on healthy human subjects (31 with the protein meal and 25 with the fat meal) and on 15 patients with pancreatic disease (10 with the protein meal and 9 with the fat meal). In 14 of the 15 cases the presence of pancreatic disease had been confirmed at laparotomy. The curves obtained after the protein meal from all but one of the 10 patients showed lower blood ^{131}I levels than those from the controls, the levels being inversely related to the severity of the pancreatic disease. Similarly, after the fat meal the levels in all the 9 patients tested were lower than in the controls. It is concluded that this test is of potential diagnostic value in suspected pancreatic insufficiency, its sensitivity being probably greater when the fat meal is used, although the large functional reserve of the pancreas may mask early or slight dysfunction of the organ. The test will not distinguish between inflammatory and malignant disease. *T. J. Thomson*

Cardiovascular System

382. **The Measurement of Portal Pressure by Liver Puncture.** (La mesure de la pression portale par ponction du foie)
A. LEMAIRE and E. HOUSSET. *Presse médicale* [*Presse méd.*] **63**, 1063–1064, July 23, 1955. 1 fig., 20 refs.

The authors describe a method of estimating the pressure in the portal vein by percutaneous puncture of the liver with a needle and measurement of the intrahepatic pressure. The needle, which is introduced for a distance of 1 to 2 cm. into the liver parenchyma, is connected through rubber tubing filled with saline to a manometer. In 26 patients with cirrhosis of the liver, with or without ascites, the intrahepatic pressure ranged from 27 to 45 (mean 34) cm. H_2O, whereas in 20 normal subjects pressure ranged from 7 to 13 (mean 11) cm. H_2O. In some cases intrasplenic pressure was measured simultaneously and the two results showed good agreement.

The authors suggest that the method may be of value in the diagnosis of portal hypertension, and that the finding of a high splenic pressure associated with a normal hepatic pressure might indicate extrahepatic obstruction of the portal vein. *P. C. Reynell*

383. **Bacterial Endocarditis in the Aged**
J. B. WALLACH, M. GLASS, L. LUKASH, and A. A. ANGRIST. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 1206–1213, June, 1955. 25 refs.

A review of the findings in 8,676 consecutive necropsies at the Queens General Hospital, Jamaica, New York, between 1936 and 1950 revealed 129 cases of bacterial endocarditis, in 82 of which there was underlying rheumatic heart disease. Of these 82 patients, 13 were over 50 years of age, the endocarditis being acute in 7 of them. [Only 5 patients were 65 or over, and of these, 4 had acute and one subacute bacterial endocarditis.] Of the 47 patients with the "non-rheumatic" form of the disease, 17 were over 50 years of age, and of these, 15 had acute and 2 subacute endocarditis. [In this group 5 patients were 65 or over and all of them had acute endocarditis.]

The authors come to the following conclusions. (1) The increasing number of older people in the population will increase the proportion of cases of bacterial endocarditis superimposed on "non-rheumatic" heart disease due to senile alterations in the collagen. (2) The diagnosis of bacterial endocarditis in the elderly may be extremely difficult because of the presence of other and more dramatic conditions which may confuse the clinical picture, with the result in such cases that the appropriate antibiotic treatment may not be given. (3) In older patients the endocarditis "often represents only an incidental terminal infection and . . . actually plays little real part in the basic primary mechanism of death". *P. D. Bedford*

CHRONIC VALVULAR DISEASE

384. **The Diagnosis of Tricuspid Stenosis**
W. WHITAKER. *American Heart Journal* [*Amer. Heart J.*] **50**, 237–241, Aug., 1955. 4 figs., 7 refs.

Discussing the importance of accurate diagnosis of tricuspid valvular stenosis in view of possible surgical treatment, the author states that the diagnosis of this lesion on clinical signs alone is difficult, especially if it is accompanied by mitral stenosis, as is usually the case. The blood-pressure readings obtained at the City General Hospital, Sheffield, by catheterization of the right side of the heart in a patient with a normal tricuspid valve are recorded and compared with those in 3 patients with both mitral and tricuspid stenosis. In all 3 cases of tricuspid stenosis pressure in the right atrium was higher than in the right ventricle during ventricular diastole, and this abnormal pressure gradient across the tricuspid valve appears to be a most valuable sign of tricuspid stenosis. The author also draws attention to the diagnostic importance of giant "a" waves—produced by the abnormal auricular pulse pressure—in the jugular venous pulse of patients with mitral stenosis. He concludes that when, in the absence of pulmonary hypertension, these two signs are present in a patient with sinus rhythm, a confident diagnosis of tricuspid stenosis can often be made. It is noted, however, that the second sign disappears if auricular fibrillation develops. *J. B. Wilson*

385. **Studies in Mitral Stenosis. VI. Pulmonary Vessels in Mitral Stenosis**
K. BÜLOW, G. BIÖRCK, O. AXÉN, H. KROOK, H. B. WULFF, and S. WINBLAD. *American Heart Journal* [*Amer. Heart J.*] **50**, 242–259, Aug., 1955. 1 fig., 40 refs.

In a study of the changes in the lungs and pulmonary vessels in patients with mitral stenosis, which was carried out at Allmänna Sjukhuset, Malmö, and the University of Lund, Sweden, various methods were used to determine the pre- and post-operative state of the lungs in 50 such patients. The relationship between the anatomical changes in the lung, as determined at post mortem or by means of lingular biopsy examination, and the clinical and the radiological findings was examined, and an attempt then made to correlate these findings with the duration of the pulmonary symptoms and the clinical results of valvotomy (in most cases digital commissurotomy).

The authors' methods of investigation and findings are given in detail. Among their more interesting conclusions were: (1) that angiopneumography is more reliable in detecting the presence of pathological conditions in the lung than lingular biopsy; (2) that in all fatal cases and also in the majority of patients with severe pulmonary complications the lungs were morpho-

logically abnormal; (3) that determination of the level of arterial oxygen saturation is one of the most informative preoperative procedures in these cases.

J. B. Wilson

386. **Factors Influencing the Late Results of Mitral Valvuloplasty for Mitral Stenosis**
L. B. Ellis and D. E. Harken. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 133–142, July, 1955. 5 refs.

The results of mitral valvuloplasty in 500 patients are reviewed, with particular reference to the influence on its outcome of certain unfavourable features—namely, age over 40 years, the presence of auricular fibrillation, significant aortic or mitral incompetence, an estimated mitral valve area before operation of more than 1 sq. cm. or after operation of less than 2·5 sq. cm., and calcification of the valve.

There were 58 operative deaths in the series, but the authors state that the mortality has been less in cases treated since the completion of the present series. Of the patients surviving operation, 442 were followed up for an average period of 22 months (range 6 months to 5 years). There was marked to moderate improvement after operation in 78% of cases. In 90 patients none of the adverse features referred to above was present, and almost all of these improved. With an increasing number of adverse factors the outcome was progressively more unsatisfactory, and only half of the patients with all these features improved. [This implies that even in patients who are not ideal subjects for operation there is a good chance of improvement.]

Embolism had already occurred in 79 patients, and all except 8 of these were in auricular fibrillation at the time of operation; embolism occurred at the time of operation in 17 of the remaining 71. After operation embolism was rare, occurring in only 5 of the 442 survivors, which suggests that the risk of this complication may be lessened by surgery. *J. A. Cosh*

387. **Correlation of Pulmonary Arteriolar Resistance with Pulmonary Vascular Changes in Patients with Mitral Stenosis before and after Valvulotomy**
F. Goodale, G. Sanchez, A. L. Friedlich, J. G. Scannell, and G. S. Myers. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 979–983, June 9, 1955. 4 figs., 11 refs.

It has been suggested by some workers that in the treatment of mitral stenosis severe pulmonary changes, in the form of alveolar fibrosis and intimal fibrosis in the small blood vessels, vitiate or even preclude the beneficial effects of valvotomy. The present authors take a more optimistic view, and at Massachusetts General Hospital have operated successfully in all types of case. In this paper they correlate the results of operation with the histological changes found in a biopsy specimen in each of 50 cases, 16 in males and 34 in females. The "pulmonary arteriolar resistance" was calculated in all cases before operation, and again from 5 to 28 months after operation in 16 of them. Pulmonary arteriolar resistance is defined as the difference between pulmonary arterial pressure and pulmonary "capillary" pressure (that is, the end-pressure in a catheter wedged in the smaller branches of the pulmonary arterial tree) divided by the cardiac index (that is, the cardiac output per minute per sq. metre body surface). The area of the mitral orifice was also measured and the biopsy specimen taken from the anterior border of the left upper lobe of the lung.

Some correlation was found between the pulmonary arteriolar resistance before operation and the degree of vascular fibrosis, but not the degree of alveolar fibrosis, present. In all but one of the 16 patients studied postoperatively there was a fall in pulmonary arterial pressure, and in all but 2 (in whom it had been very low) there was a fall in arteriolar resistance. The authors conclude that the poor correlation between the severity of the preoperative pulmonary resistance and the pathological changes in the lung indicates that vasoconstriction is an important factor in producing pulmonary hypertension in mitral stenosis. They consider that in most cases the increased pulmonary resistance is reversible and hence that relief of the stenosis by valvotomy should be undertaken whatever the severity of the preoperative hypertension. *Donald McDonald*

388. **The Effects of Mitral Valvuloplasty on Cardiovascular and Renal Function at Rest and during Exercise**
W. E. Judson, J. D. Hatcher, W. Hollander, and M. H. Halperin. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 1297–1311, Aug., 1955. 2 figs., 27 refs.

Cardiovascular and renal measurements were made at rest and following exercise in 9 patients with mitral stenosis before and within 2 to 32 weeks after mitral valvuloplasty. Cardiohemodynamic measurements after operation showed a slight, but not statistically significant, increase in the cardiac index, and a significant increase in the stroke index, since the heart rates tended to be slower. The pulmonary arterial and "pulmonary capillary" pressures were significantly lower. The right ventricular end-diastolic pressure was not significantly reduced at rest, but after exercise it was significantly less than before operation. The calculated "total pulmonary" resistance (which includes the resistance imposed by the mitral valve) was significantly reduced, but the "pulmonary arteriolar" resistance was not. The increase in the "pulmonary arteriolar" resistance in response to exercise was not so great after operation. The resistance opposing the right ventricle was decreased after operation apparently because of approximately equal reductions in the resistance of the pulmonary vessels and that imposed by the stenosis of the mitral valve. There was a slight reduction in the work of the right ventricle and a slight increase in the work of the left ventricle after operation but neither was statistically significant.

Preoperative resting renal plasma flow was approximately half and glomerular filtration rate about four-fifths of normal values. After operation the resting renal plasma flow and glomerular filtration rate were both increased, on the average, by about one-sixth, the latter approaching normal. In response to exercise the renal

plasma flow fell, on the average, 43% before operation and only one-half that much after operation, a significant improvement. The glomerular filtration rate decreased in response to exercise, on the average, 38% before operation and only about two-thirds that much after operation. This improvement was not statistically significant. The considerable decreases in urine flow, excretion of sodium, chloride, and potassium in response to exercise, which tended to parallel the changes in the glomerular filtration rate, were not significantly different in magnitude after operation as compared with before. Although all the renal functions tended to recover from exercise more rapidly after operation, the mean data showed no significant differences from the preoperative responses.

In this group of patients mitral valvuloplasty produced varying degrees of improvement in the cardiovascular and renal functions both at rest and after exercise. In none of the patients, however, did the cardio-renal hemodynamic measurements return to normal values. A general improvement in cardiovascular function in individual patients was sometimes associated with increases in renal plasma flow, glomerular filtration rate and the ability to excrete salt and water during and after exercise. However, postoperative increases in salt and water excretion could not be consistently correlated with any specific change in cardiovascular or renal function, or both.—[Authors' summary.]

389. **Mitral Commissurotomy in Relation to Pregnancy**
R. P. GLOVER, D. E. MCDOWELL, T. J. E. O'NEILL, and O. H. JANTON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 895–900, July 16, 1955. 19 refs.

In this paper from the Presbyterian Hospital, Philadelphia, the authors describe 5 cases in which mitral commissurotomy was performed during pregnancy and comment on 6 others in which pregnancy occurred after this operation. While admitting that the series is small, the authors report these cases "in order to give encouragement to others faced with the decision for or against surgery". The first patient in the present series was operated on at 6½ months, but the authors point out that according to the criteria they now adopt the operation should have been performed earlier or not at all. There was, however, remarkable relief of symptoms in this case, followed by easy delivery. The second patient, who underwent commissurotomy for severe orthopnoea and pulmonary congestion, continued to term and was delivered without difficulty. In the third case the operation was performed at one month and the patient had no cardiac symptoms subsequently. The fourth patient had a spontaneous abortion at the 12th week, just 6 weeks after commissurotomy. In the fifth case failure had occurred in two previous pregnancies with increased cardiac symptoms afterwards. After commissurotomy in the 6th week of the third pregnancy there were no cardiac symptoms and the patient was delivered easily at full term.

The authors consider these cases to show that mitral commissurotomy can be carried out safely during pregnancy and therapeutic abortion and sterilization avoided. Pregnancy after the operation is, as a rule, uncomplicated, but the patient should be closely watched by a cardiologist. They have performed commissurotomy in 500 consecutive cases of mitral stenosis, and from that considerable experience they offer the following tentative criteria for the selection of cases suitable for the operation during pregnancy: "(1) Mitral commissurotomy is not advisable during pregnancy except in patients in Stages 3 and 4." [New York Heart Association classification.] "Patients in Stages 1 and 2 can be safely carried through pregnancy and delivery by a strict medical regimen. (2) Patients in Stages 3 or 4 should have an exploration of the valve and commissurotomy before a therapeutic abortion and sterilization are considered. (3) Commissurotomy, if it is indicated, is best done in the first trimester, when the cardiac load is less . . . as a rule it is contraindicated after the 32nd week. (4) Mitral commissurotomy should be carried out during pregnancy if repeated emboli are endangering the life of mother and child; the operation is then an emergency and a life-saving procedure. (5) In patients over 35 years of age or in those with auricular fibrillation the condition of the valve found at surgery and the response after commissurotomy may be used to indicate whether the pregnancy represents too great a threat to the patient's life." Finally, the authors point out that the rigidity of the valve, the degree of regurgitation, the size of the cardiac chambers, and the presence or absence of left atrial thrombi, which can be assessed accurately by exploration, are among the more important factors determining the advisability of the continuation of the pregnancy and of others in the future.

D. P. McDonald

CONGENITAL HEART DISEASE

390. **Surgical Closure of Interatrial Septal Defects by Circumclusion.** [In English]
T. SØNDERGAARD, H. GØTZSCHE, P. OTTOSEN, and J. SCHULTZ. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **109**, 188–196, July 23, 1955. 8 figs., 7 refs.

After a concise review of the methods devised by various previous workers for closing interatrial defects the authors describe in detail their own method and present a report on 6 patients successfully treated at the Kommunehospital, Aarhus, Denmark. Essentially, the method consists in blunt dissection into, and development of, the cleavage plane which is present between the muscular walls of the right and left atria and which is filled with loose connective tissue. When this is completed the right index finger is inserted into the right atrium through the auricle and the extent of the defect explored. A curved blunt probe is placed at the upper end of the cleavage and, with very slight pressure, is guided along the lower edge of the defect until it appears at the lower end in the pad of fat situated between the atria and the coronary sinus. An oiled silk No. 10 suture is then secured to the tip of the probe and gently pulled back along the groove as the probe is withdrawn, the two free ends of the suture being tied over a piece of

gelatin sponge at the lower end of the cleavage. As the suture is pulled tight the right index finger in the right atrium feels the defect becoming smaller and smaller and finally closing (" circumclusion ").

The ages of the 6 patients subjected to this operation ranged from 4 to 33 years. All were improved by the operation, and subsequent cardiac catheterization in 4 of them revealed complete closure of the defect, with normal intracardial pressures. *C. A. Jackson*

391. **The Operative Management of Pulmonary Valvotomy for Pulmonary Valve Stenosis with Normal Aortic Root**

B. B. MILSTEIN and R. BROCK. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 1–18, 1955. 10 figs., 2 refs.

392. **The Direct-vision Intracardiac Correction of Congenital Anomalies by Controlled Cross Circulation. Results in Thirty-two Patients with Ventricular Septal Defects, Tetralogy of Fallot, and Atrioventricularis Communis Defects**

C. W. LILLEHEI, M. COHEN, H. E. WARDEN, and R. L. VARCO. *Surgery* [*Surgery*] **38**, 11–29, July, 1955. 3 figs., 15 refs.

The use of controlled cross-circulation methods has enabled operations to be performed under direct vision on the interior of the heart in 32 cases since March, 1954, at the University of Minnesota Hospitals, Minneapolis.

The authors calculate that if the patient's heart is to be excluded for any period of time from the circulation, a volume of blood varying between 25 and 40 ml. per kg. body weight per minute has to be circulated, which is considerably less than has previously been thought to be necessary. However, experimental results in dogs have suggested that as little as 8 to 14 ml. per kg. per minute would be adequate to maintain life—a figure that is less than one-tenth of the resting cardiac output—but that to avoid undue irritability of the heart a somewhat larger flow is needed. The principle of the cross-circulation technique employed is to take blood from the descending aorta of a donor through a catheter introduced through the femoral artery and to pass this by means of a pump into the base of the patient's aorta. The return flow from the patient is obtained from both venae cavae through catheters inserted through stab wounds in the right atrium; the blood is led to a venous reservoir with an air trap and returned via a second pump to the femoral vein of the donor. [For details of the technique the reader is referred to the original article.]

By using the very much lower rate of flow into the patient's aorta than has previously been thought necessary the authors have overcome the difficulty of the coronary venous return, which at higher rates will tend to obscure the operation field. On the other hand with a low rate of flow the pressure is often not enough to shut the aortic valves, with the result that a leak from the aorta into the ventricle occurs unless a tourniquet is passed round the base of the aorta and tightened.

The use of the cross-circulation technique has so far been confined to the surgical correction of congenital abnormalities. Of 22 cases of interventricular septal defect treated, the operation was successful in 15. Of the 7 deaths, 6 occurred in infants under 2 years of age. Six cases of the tetralogy of Fallot have been treated, the stenosis being resected and the ventricular defect being closed at the same time; 3 of these patients survived. Four patients with other congenital defects have also been operated on, 2 surviving. The patients were all grossly incapacitated at the time of operation, which would not have been considered a practical proposition without the cross-circulation technique. The donors suffered no ill-effects except in 2 cases—one in which severe hypotension developed and required cardiac massage, and another in which air embolism produced transient neurological sequelae.

[This communication is one of the most important contributions yet made to cardiac surgery and should be read in detail by anyone interested in the subject. The question will be raised as to how far and to what extent donors can be used without exposure to risk, but that will be a problem for the individual surgeon to decide. The use of a human donor is certainly a great advance on cross-circulation methods which involve animals, and although the authors' technique may not ultimately prove to be the ideal method, it does open up a wide new field.] *T. Holmes Sellors*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

393. **The Physiologic and Pathologic Evaluation of the Implantation of the Internal Mammary Artery into the Left Ventricular Myocardium for the Treatment of Coronary Artery Disease**

A. A. BAKST, R. MANIGLIA, A. ADAM, and C. P. BAILEY. *Surgery* [*Surgery*] **38**, 349–362, Aug., 1955. 6 figs., 18 refs.

In animals in which the internal mammary artery had been implanted into the ventricular myocardium for 6 months, retrograde blood flow from the distal cut end of the ligated left anterior descending coronary artery averaged 2·3 c.c. per minute, representing a normal amount of the intercoronary arterial anastomotic flow. This intercoronary anastomotic flow was demonstrated to arise almost entirely from the nonoccluded circumflex artery. No increase or change in the intercoronary anastomotic flow could be attributed to the implanted internal mammary artery.

Pathologically, the lumina of the implanted vessels were 95% obliterated by the severe intimal proliferation. The vessels were surrounded by fibrous tissue and presented a picture which suggested that they had been walled off by the ventricular myocardium, much the same as a foreign-body reaction. Although a few fine periadventitial vessels were demonstrated, they were believed to be due to terminal phases of the inflammatory reaction. They were small and sparse and were not physiologically significant.

We were unable to demonstrate that a systemic artery implanted into the ventricular myocardium for 6 months could materially increase or contribute to the extra-

intercoronary collateral anastomotic flow of the interrupted left anterior descending artery.—[Authors' summary.]

394. **Effects of Lipotropes and Sitosterol on the Level of Blood Lipids and the Clinical Course of Angina Pectoris**
C. F. WILKINSON. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 3, 381–388, June, 1955. 3 figs., 12 refs.

The author has made many attempts to find a satisfactory substance capable of lowering the blood cholesterol concentration in normal human subjects and in patients with hypercholesterolaemia. In this paper from New York University Post-Graduate Medical School he reports the results of his latest attempt, in which the effect of a mixture of choline and inositol was compared with that of a placebo, each given over 4 to 6 months to 40 out-patients suffering from angina pectoris, the patients being asked to record daily on a special card the degree of cardiac pain and the number of trinitrin tablets taken. The blood cholesterol and phospholipid levels were estimated every 3 weeks. On clinical grounds no significant difference between the groups was detectable, and the estimations showed that the blood lipid levels in the treated group were slightly higher than in those taking the placebo.

Since it has been reported that sitosterol added to the diet of cholesterol-fed rabbits reduced the expected increase in blood cholesterol levels, a metabolic experiment was carried out in which 8 patients were given gamma sitosterol equivalent to 15 to 30 g. of soya sterol daily with their meals for up to 35 weeks; the results showed that sitosterol had no reducing effect on the serum cholesterol level. The author comments that further work on purified phytosterols is necessary.

J. N. Agate

395. **Postoperative Myocardial Infarction. Report of Twenty-five Cases**
F. WASSERMAN, S. BELLET, and R. P. SAICHEK. *New England Journal of Medicine* [*New Engl. J. Med.*] 252, 967–974, June 9, 1955. 3 figs., bibliography.

The increasing age of the population and recent advances, particularly in the fields of anaesthesia, antibiotics, and methods of postoperative care, have resulted in an increasing number of operations on old people, with a concomitant increase in the incidence of cardiac complications following surgical procedures. In a series of 37,000 operations (60% major, 40% minor) performed between 1948 and 1954 at the Graduate Hospital of the University of Pennsylvania, Philadelphia, there were 25 cases of postoperative myocardial infarction (0·07%). The average age of these patients was 64·6 years, and 19 of them had shown evidence of heart disease preoperatively. There were 5 deaths among these patients, 3 of them directly the result of the infarction.

The presenting symptoms were rather unusual; only 12 of the 25 suffered from precordial pain, which in 8 cases was typical and in 4 was atypical in distribution. In 10 cases a persistently low blood pressure (systolic pressure less than 90 mm. Hg) was the only sign (apart from characteristic changes in the electrocardiogram) which was suggestive of myocardial infarction; in the remaining 3 cases there were no premonitory signs of any kind. Treatment was along standard lines. It is suggested that as a prophylactic measure a thorough cardiological investigation should precede surgical operations in elderly patients wherever possible.

Donald McDonald

396. **Myocardial Infarction in Women**
T. N. JAMES, H. W. POST, and F. J. SMITH. *Annals of Internal Medicine* [*Ann. intern. Med.*] 43, 153–164, July, 1955. 4 figs., 27 refs.

An analysis is presented of 146 cases of myocardial infarction in women seen at the Henry Ford Hospital, Detroit, over a 4-year period. The initial attack occurred most commonly in the sixth, seventh, and eighth decades; only 11 of the patients were still menstruating and 7 were under 45 years of age. Associated conditions were hypertension in 71 patients, diabetes in 14, and hypertension with diabetes in 17; of the 11 patients with onset before the menopause, 8 had hypertension or diabetes or both. In 3 cases the menopause occurred within a year of the attack. Other contributory factors were rheumatic heart disease with coronary embolism in one case and polycythaemia in another.

The authors point out that myocardial infarction before the menopause is unusual, and is rare in the absence of such contributory factors as hypertension and diabetes. The " protective " effect of oestrogens is discussed.

J. A. Cosh

HEART FAILURE

397. **Vena Cava Inferior Ligation in Congestive Heart Failure. Report on 100 Cases in Five Years**
J. BERNATH, R. GUILLEMOT, P. SAMUEL, and R. HEIM DE BALSAC. *American Heart Journal* [*Amer. Heart J.*] 50, 112–128, July, 1955. 2 figs., 31 refs.

The authors discuss the indications for, and the results of, the operation of ligation of the inferior vena cava, with reference to the first 100 cases so treated at the Hôpital Broussais, Paris, between 1949 and 1953, the maximum period of follow-up thus being about 5 years. Two-thirds of the patients had mitral valvular lesions, and half were suffering from serious congestive failure, with decubitus dyspnoea, oedema, and enlarged liver, and had derived no appreciable benefit from medical treatment. Other indications were right ventricular failure, with or without repeated pulmonary emboli or acute pulmonary oedema, and (in 10 cases) left ventricular failure. The preparation of the patient for operation is discussed, particular stress being laid on the regulation of fluid balance. It is the authors' custom to induce differential sympathetic block by intraspinal injection of procaine; this produces effects similar to those of caval ligation and, as a preliminary procedure, may reduce the risk of the operation. The problem of anaesthesia for these patients is a complex one, and various forms of local or spinal analgesia have been tried, but latterly

the authors have preferred general anaesthesia. The approach is by the transperitoneal route, and despite the exercise of great care, retroperitoneal haematoma is a common and often serious complication. In general the authors do not recommend the operation for patients under the age of 30, although the present series included 11 such patients.

Of the 100 patients, 13 died at operation or within one week, and a further 27 within one year; the remaining 60 were improved, many being able to return to work. The immediate effects of the operation are good: dyspnoea is lessened and the patient can once again sleep lying down, the hepatomegaly regresses, and there is diuresis, with reduction of the oedema. Later, however, a collateral circulation develops slowly over many months, gradually diminishing the effect of the ligation. Four patients died after the first year, and 9 others deteriorated, but of 33 patients operated on 4 years ago 11 are alive, the condition of 8 being quite satisfactory. Treatment by diet and drugs must be maintained, of course, since the ligation is a palliative measure only.

[This operation is not popular in Great Britain.]

M. Meredith Brown

398. **The Influence of Advanced Congestive Heart Failure on Pulsus Alternans**

J. M. RYAN, J. F. SCHIEVE, H. B. HULL, and B. M. OSER. *Circulation* [*Circulation* (*N.Y.*)] **12**, 60–63, July, 1955. 3 figs., 4 refs.

In 3 patients with left ventricular failure pulsus alternans was observed to diminish or disappear simultaneously with clinical deterioration and to increase with clinical improvement. Decrease in the venous return to the heart is known to exaggerate pulsus alternans, and exercise and venous infusions to diminish it. It is suggested that a certain critical range of ventricular filling pressure is necessary for the manifestation of pulsus alternans. As the filling pressure rises, the greater and more uniform diastolic stretch of the ventricular muscle may possibly promote more uniform contractions.

J. McMichael

399. **The Effect of Exercise on the Excretion of Water by Patients with Congestive Failure**

L. E. DUNCAN. *Circulation* [*Circulation* (*N.Y.*)] **12**, 90–95, July, 1955. 3 figs., 11 refs.

Patients with congestive heart failure often excrete small amounts of hypertonic urine even after the ingestion of water, and this contributes to the development of hyponatraemia. In experiments carried out at the U.S. National Heart Institute, Bethesda, Maryland, to determine whether exercise increases this tendency, 6 subjects with heart disease and 2 healthy subjects were given a water load of 20 to 40 ml. per kg. body weight, 5 to 10 ml. per kg. being drunk at half-hourly intervals during the 2 hours preceding the period of test diuresis. In the normal subjects mild exercise (walking) had little influence on either the high, sustained rate of urine flow or on the solute content of the urine. In patients with mild cardiac failure exercise induced a marked decrease in the rates of urine flow and solute elimination, though the concentrations of urea and sodium in the urine were usually not much changed. These findings suggest that the changes resulted from a decrease in the glomerular filtration rate. In some patients, however, there was an increase in the concentration of urinary solutes during the period of low urinary output, and the possibility that this was due to pituitary antidiuretic hormone cannot be excluded.

It is surmised that these experiments illustrate possible mechanisms whereby hyponatraemia is maintained in advanced heart failure.

J. McMichael

400. **Electrolyte Studies in Heart Failure. I. Cellular Factors in the Pathogenesis of the Edema of Congestive Heart Failure. II. Extracellular Factors in the Pathogenesis of Congestive Edema**

L. T. ISERI, A. J. BOYLE, D. E. CHANDLER, G. B. MYERS, and I. J. MADER. *Circulation* [*Circulation* (*N.Y.*)] **11**, 615–619 and 620–627, April, 1955. 43 refs.

The findings reported in these two papers from Wayne University College of Medicine, Detroit, were based on analyses of deltoid muscle samples and of blood plasma obtained from patients during a period of congestive heart failure and again later after cardiac compensation was restored. Analysis of the muscle tissue showed that during congestive failure its potassium content was only 30·1% of the subsequent level; no change in the intracellular water content was demonstrated.

In a further study the plasma electrolyte levels were determined on two groups of patients with congestive cardiac failure: in the first group after the patients had received 4 g. of sodium chloride in water by mouth and had then performed certain physical exercises; in the second group the observations were first made early in the morning, while the patients were in the basal state, and then repeated in the evening after a day of unrestricted exercise and food intake. Both groups showed a significant rise in the plasma sodium concentration after exertion. This was interpreted as indicating an elevation of extracellular osmolarity which in turn reflected a rise in intracellular osmolarity.

H. Payling Wright

HYPERTENSION

401. **Fundus Changes in Hypertension in Relation to Postmortem Systemic Alteration**

M. PUIG SOLANES, J. A. QUIROZ, and G. G. BARRIENTOS. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **39**, Part II, 137–147, April, 1955. 4 figs., 30 refs.

An analysis at the National Institute of Cardiology of Mexico of the findings in the optic fundus and at necropsy in 40 cases of essential hypertension and 40 of chronic glomerulonephritis revealed that there was no qualitative difference in the eye grounds of the two groups, but that there was a significant difference in the average number of oedematous lesions, which was greater in the nephritic group. This preponderance, which may possibly be the result of the toxic factor, was not directly related to the disturbance of blood chemistry in the nephritic cases and the eye changes were not qualitatively related to the degree of nephrosclerosis. No

significant difference was seen between the fundal appearances in severe benign and malignant hypertension. No correlation was found between the severity of changes in the eye and the brain, but some correlation was noted between the degree of change in the eye and in the kidneys and heart.

J. E. M. Ayoub

402. Analysis of 177 Cases of Hypertensive Vascular Disease with Papilledema. One Hundred Twenty-six Patients Treated with Rice Diet

B. NEWBORG and W. KEMPNER. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 33–47, July, 1955. 3 figs., 22 refs.

The authors have reviewed the clinical course of every case of malignant hypertension with papilloedema, 177 cases in all, seen at the medical clinic of Duke University School of Medicine, Durham, North Carolina, between 1942 and 1953. Patients thought to have had chronic nephritis before the development of their hypertension and those with polycystic kidney were excluded. An attempt was made to treat every patient with the Kempner rice diet, but 18 refused and 33 had to discontinue the treatment because of electrolyte imbalance. Out of the remaining 126 cases there were 100 in which the clinical records and dietary supervision were considered adequate for assessment of the efficacy of the treatment. If the rice diet is strictly followed the urinary excretion of chloride should be only 5 to 15 mg. per 100 ml. in a 24-hour collection.

Of 39 patients in whom supervised treatment lasted less than one year, 7 died during treatment and only 6 (19%) of the remaining 32 are alive. Of the 61 patients supervised for over a year, 18 discontinued treatment after one to 7½ (average 3) years, and of these, 9 (50%) are still living, while 43 continued treatment and 37 (83%) are still living (average 4 years). The survival rate was thought to be related to the degree of renal impairment, as judged by the phenolsulphonephthalein excretion test. The papilloedema was found to have disappeared in 92 out of 100 patients maintained on the strict or slightly modified rice diet after an average of 5 months.

[Statistical analysis of the differences between the groups would have been helpful. Although the rice diet is undoubtedly beneficial in these patients—for whom before such treatment was available the prognosis was extremely poor—it is unpleasant and the results achieved by it demand careful comparison with those obtained with the alternative therapy now available with various hypotensive drugs.] *P. Hugh-Jones*

403. Influence of Emotional Variables in Evaluation of Hypotensive Agents

A. P. SHAPIRO. *Psychosomatic Medicine* [*Psychosom. Med.*] **17**, 291–305, July–Aug., 1955. 10 figs., 20 refs.

The influence of variables created by emotional factors in patients with hypertension during treatment with various drugs, including "veriloid" and salts of hexamethonium, was studied at the University of Texas, Dallas. From his observations the author concludes that changes in blood pressure and symptoms during treatment are often due not to the drug itself, but to the emotional influence of admission to hospital, the doctor–patient relationship, and the patient's life circumstances.

[This paper shows yet again that attempts to appraise the effect of drugs without regard to the patient's emotional state are unscientific and misleading.]

Desmond O'Neill

404. Comparison of Rescinnamine and Reserpine as Hypotensive Agents

F. H. SMIRK and E. G. MCQUEEN. *Lancet* [*Lancet*] **2**, 115–116, July 16, 1955. 8 refs.

The authors report from the University of Otago Medical School, New Zealand, that in the treatment of hypertension they have found that reserpine when given alone in daily doses of 0·5 to 1·0 mg. is mildly hypotensive, but when combined with pentolinium (pentapyrrolidinium) a potentiation of the activity of the latter compound was observed. This has allowed a reduction of the dose of pentolinium, with a consequent diminution in the incidence and severity of side-effects. However, about 10% of patients who received reserpine either alone or in combination with pentolinium experienced substantial degrees of mental depression.

The authors have therefore tried another, recently isolated, alkaloid of *Rauwolfia serpentina*, rescinnamine, which they substituted for reserpine in the treatment of 32 patients over periods of 4 weeks to 4 months. It was found that the change to rescinnamine resulted in no important loss of control of the blood-pressure, the hypotensive effects of reserpine and rescinnamine being similar whether the drugs were used alone or in combination with pentolinium. One advantage to be gained by the change was that mental symptoms occurring in patients receiving reserpine, such as depression and lassitude, were relieved by changing to rescinnamine; a disadvantage of rescinnamine was that it caused anorexia and abdominal discomfort, and in a few cases insomnia and a feeling of tension. Subjectively, 13 of the patients preferred rescinnamine, 12 reserpine, and 7 were indifferent. *R. Wien*

405. Lumbar Sympathectomy in the Treatment of Hypertensive Ischemic Ulcers of the Leg (Martorell's Syndrome)

J. PALOU. *Circulation* [*Circulation (N.Y.)*] **12**, 239–241, Aug., 1955. 1 fig., 10 refs.

The treatment by lumbar sympathectomy at the Instituto Policlinico, Barcelona, of 4 cases of hypertensive ulceration of the leg is described. The patients were all women in the sixth decade of life who had severe arterial hypertension. The lesions, which in 3 cases were bilateral, began as bluish-red, flat, painful spots on the outer aspect of the lower part of the leg, which became superficial, painful ulcers unrelieved by rest. Some had healed, leaving scars. In no case was there evidence of venous disease, nor were the peripheral pulses impaired.

In each case lumbar sympathectomy was performed and was followed by healing in about 2 months; in one

case it is mentioned that pain was relieved immediately by the operation. The lesions, which were first described by Martorell in 1945, are stated to be due to obliterative lesions of the arterioles similar to those met elsewhere in essential hypertension.

[Martorell's name is also associated with an entirely different syndrome which is due to obliteration of the arteries arising from the arch of the aorta.]

C. J. Longland

BLOOD VESSELS

406. Effects of Restriction of Dietary Fat and Cholesterol upon Serum Lipids and Lipoproteins in Patients with Hypertension

F. T. HATCH, L. L. ABELL, and F. E. KENDALL. *American Journal of Medicine* [*Amer. J. Med.*] **19**, 48–60, July, 1955. 2 figs., 26 refs.

Working at the Goldwater Memorial Hospital (Columbia University), New York, the authors have taken advantage of the therapeutic use of the Kempner rice diet in the treatment of hypertension to study the effects of the drastic reduction of fat (to 3 g. per day) and complete elimination of cholesterol intake which this diet entails on the levels of lipoprotein and neutral fat in the serum. The serum levels in 44 patients during a control period of 4 to 18 weeks on a diet poor in salt but of normal fat content (85 g. per day) were compared with those during periods ranging from 4 to 20 weeks on the Kempner diet. Similar observations were made on smaller groups of patients receiving diets providing intermediate amounts of fat and cholesterol. The composition of the various diets is described.

During the control period the serum lipid levels in these hypertensive patients differed little from those in a series of healthy ambulatory subjects. Only during the administration of the unmodified Kempner diet was there a statistically significant reduction in the mean blood cholesterol level, and then by only 15%, that is, not below the normal range of values. Investigation of the behaviour of the different groups of serum lipoproteins showed no significant alteration in the concentration of the S_f 12–20 lipoprotein fractions, but a statistically significant increase (nearly double) in the concentration of the S_f 20–100 fractions during the period on the rice diet. All the changes seemed to depend on the restriction of fat rather than on the elimination of cholesterol, but even on the diet severely reduced in fat content some patients showed a lipaemia, with significant increase in the serum neutral fat content.

[These results suggest that simple dietary measures are unlikely to be of much help in the prevention or treatment of atheroma. Virtual elimination of fat from the diet produces only a small reduction in the serum lipid level and, as the authors observe, carbohydrate and protein appear to be readily used for the endogenous synthesis of fat. Gofman *et al.* (*Circulation*, 1950, **2**, 161) found a reduction in the serum concentration of S_f 10–20 lipoproteins following reduced fat intake.]

P. Hugh-Jones

407. Fat Tolerance and Arteriosclerosis. (Die Bedeutung alimentärer Fettbelastungen für die Diagnose der Arteriosklerose)

G. SCHETTLER and H. JOBST. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 1077–1081, July 22, 1955. 3 figs., 41 refs.

Fat tolerance was studied at the University Medical Clinic, Marburg, in 10 healthy subjects with a mean age of 28, in another 10 healthy persons with a mean age of 54, and in 10 " arteriosclerotic " patients with a mean age of 53; all the " arteriosclerotics " had had at least one recent attack of coronary occlusion. A meal was given consisting of 0·5 g. butter per kg. body weight with 100 g. of bread and about 150 ml. of malt coffee. Specimens of venous blood were taken before the meal and 1¼, 2½, 2¾, and 5 hours after it for the measurement of its turbidity and chylomicron count, and for the estimation of its neutral fat, phospholipid, free cholesterol, and cholesterol ester content.

The serum phospholipid and cholesterol levels after the fatty meal were not appreciably different in the two control groups. The serum turbidity, neutral fat level, and chylomicron count were, however, higher after the meal in the older control group than in the younger. In patients with " arteriosclerosis " the serum free cholesterol, cholesterol ester, and neutral fat levels and the chylomicron count were significantly higher after the meal than in either control group, although the serum phospholipid level was unchanged in all three groups. Furthermore, in the " arteriosclerotic " group the return of the serum turbidity, chylomicron count, and neutral fat content to normal levels was grossly delayed. The authors suggest that the estimation of serum turbidity and neutral fat content, together with the chylomicron count, after a fatty meal provides a suitable diagnostic test for " arteriosclerosis ".

[In the Anglo-American literature the form of arterial disease characterized by lipid-laden, thickened intima which narrows the lumen of the arteries supplying blood to the heart, brain, kidney, and other organs is now usually termed atherosclerosis, arteriosclerosis being used as a general designation which includes, besides atherosclerosis, such conditions as Mönckeburg's sclerosis and hyperplastic arteriosclerosis. Atherosclerosis is thought by many to be a sequel of alimentary hyperlipaemia, and it was first pointed out by Moreton (*Science*, 1947, **106**, 190) that the dietary regimens current in Western countries lead to repeated bouts or showers of postprandial hyperlipaemia. He and others have further postulated that during postprandial hyperlipaemia a marked rise occurs in the number of lipid droplets of large size in the circulation, and that these chylomicrons are subject to phagocytosis by the macrophages of the intima, with the formation of intimal foam-cell plaques. It would be expected, therefore, that the degree and duration of experimentally produced hyperlipaemia would be greater in atherosclerotic patients than in healthy controls. The present authors' findings confirm those of similar work previously reported from the U.S.A. (in which, however, only the serum turbidity and lipoprotein content were studied), although no reference is made to it.]

Z. A. Leitner

Haematology

408. **Lymphoma of the Stomach and Intestine**
J. F. P. SKRIMSHIRE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 203–214, July, 1955. 5 figs., 34 refs.

The author reviews the features of 24 cases of lymphoma of the gastro-intestinal tract, of which 18 were seen at St. Thomas's Hospital, London, between 1948 and 1953 and formed 10% of all cases of lymphoma seen at the hospital in that period, suggesting that the lesion is less rare than has been supposed. In 10 cases the tumour was in the stomach and in 14 in the small intestine. The growths were classified histologically as follicular lymphoma in one case, as reticulum-cell sarcoma in 17, and as lymphosarcoma in 6, but the author points out the difficulty of making a rigid classification since the histological details often differed in different parts of the tumour and in the associated lymph nodes; for example, in one case sections of the tumour in the stomach were considered to show reticulum-cell sarcoma, whereas examination of a lymph node removed later showed the picture of Hodgkin's disease.

Clinically, the onset was often chronic with no distinguishing features, the most common complaint being "indigestion". In some cases, however, there was an acute onset with perforation, obstruction, or haemorrhage; in these the nature of the lesion was first appreciated at laparotomy. In 8 cases of gastric tumour and in 6 of intestinal tumour resection was carried out. Radiotherapy was also given, as these tumours are highly radiosensitive. The prognosis is poor in most cases, although somewhat less so when the tumour is in the stomach; even so half of the patients die within one year of diagnosis. In individual cases the prognosis is difficult to assess because some patients, especially those in whom the tumour can be resected, have lived for much longer than one year, and reports show that 10 to 15% of all patients have survived for more than 5 years. *M. C. G. Israëls*

409. **The Prognosis in Hodgkin's Disease**
A. M. JELLIFFE and A. D. THOMSON. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 21–36, March, 1955. 7 figs., 20 refs.

All cases of Hodgkin's disease (227) seen at the Middlesex Hospital, London, in recent years have been analysed in an attempt to determine those factors which influence the natural evolution of the disease. As would be expected, the prognosis is markedly dependent on the extent of the disease at the time the patient is first seen. In Stage I of the disease—involvement of lymph nodes in only one main group—59% of patients survive 5 years; in Stage II—involvement of lymph nodes in two or more adjacent groups—60% survive this period; in Stage III—more extensive disease—only 3% survive 5 years. Of the present series of patients 15 survived over 10 years, 6 being in Stage I and 9 in Stage II when first seen. The prognosis was best in patients with onset in the third and fourth decades; it was less favourable in males than in females.

Tumours were graded histologically according to the classification of Jackson and Parker into paragranuloma, granuloma, and sarcoma. The prognosis in each of these grades did not entirely substantiate the findings of the earlier workers; while it was progressively worse with the more malignant forms, it probably depended more upon the clinical stage of the disease than upon the histological grade. The authors give reasons for preferring to use the terms Grades 1, 2, and 3, the first of which is predominantly lymphocytic, the second mixed, and the third predominantly epithelial.

They were unable to determine the precise value of the treatment given to the patients in this series. The few untreated cases were largely selected in that the disease was advanced; similarly, the cytotoxic drugs were rarely given in early cases or as the primary form of treatment. Irradiation did appear to eradicate local disease for a variable and, in some cases, a considerable length of time provided the dosage was adequate. The complications are discussed. *Nigel Compston*

410. **The Thymic Origin of Hodgkin's Disease**
A. D. THOMSON. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 37–50, March, 1955. 26 figs., 41 refs.

In this study of the histogenesis of Hodgkin's disease the author propounds the theory that this condition is in reality a metastatic carcinoma of the thymus gland.

After a historical review of the various views which have been held as to the aetiology of Hodgkin's disease he draws attention to a number of cases reported in the literature in which the disease was alleged to have arisen in, or to have involved, the thymus gland. He then presents his hypothesis in detail, starting with a study of the embryology of the thymus. The gland has a mixed origin from endodermal, epithelial, and mesodermal tissues. Hassall's corpuscles, of endodermal origin, pass through a stage of development in which large mononuclear cells, "owl's eye" cells, and multinucleated giant cells appear. The mature gland also contains fibrous trabeculae, lymphocytes, and eosinophil granulocytes. At one stage of its development or another, therefore, the thymus contains all the cellular elements observed in Hodgkin's disease. The lymphatic drainage of the thymus gland is then described, the main channels passing into the neck on both sides, to the chest wall and internal mammary chain anteriorly and thence to the abdomen, and into the tracheo-bronchial group of lymph nodes—all sites which are commonly affected in Hodgkin's disease.

In a series of 275 cases of Hodgkin's disease studied at the Middlesex Hospital, London, there were 112 with a mass in the region of the thymus, a further 120 with

involvement elsewhere in the mediastinum, and only 43 in which no mediastinal masses were demonstrated. (Many of the cases in this last group, however, were not thoroughly investigated.) The histological material from this series could be divided into three grades according to the cellular appearance, as described in the previous paper by Jelliffe and the author [see Abstract 409]. Grade-1 tumours, which are similar to the paragranulomata of Jackson and Parker, are predominantly lymphocytic; Grade-2 tumours show approximately equal degrees of lymphocytic and epithelial proliferation; and Grade-3 tumours, the most malignant, are predominantly epithelial. The clinical and histological findings in 7 cases of mixed thymic tumour reported by Eisenberg and Sahyoun (*Arch. Path.*, 1950, **49**, 404; *Abstracts of World Medicine*, 1950, **8**, 603) and in 9 reported by Lowenhaupt and Brown (*Cancer (N.Y.)*, 1951, **4**, 1193) are described, and it is pointed out that histologically these tumours showed just such mixtures of lymphocytic and epithelial proliferation, while the clinical course was closely similar to that of Hodgkin's disease. The apparent absence of a thymic tumour in many cases of Hodgkin's disease is attributed by the author to failure to seek for such a tumour. Alternative explanations offered are that thymic tumours may be overlooked because of their smallness, that they may have undergone sclerosis, or that the primary tumour may have arisen in ectopic thymus tissue, which is present in about 20% of persons.

This important article is illustrated by photomicrographs of embryonic thymus tissue, adult thymus tissue, tissue showing the typical histological pattern of Hodgkin's disease, and thymic tissue removed at operation in a case of Hodgkin's disease. *Nigel Compston*

411. **Acquired Fibrinopenia in Pregnancy**

A. P. BARRY, F. GEOGHEGAN, and S. M. SHEA. *British Medical Journal* [*Brit. med. J.*] **2**, 287–290, July 30, 1955. 7 refs.

The condition of acquired fibrinopenia occurring as a complication in certain obstetrical emergencies has now been frequently described. One possible explanation of this condition is that a release of thromboplastin from the placental site into the circulation causes intravascular coagulation and depletion of fibrinogen. In this paper from the National Maternity Hospital and University College, Dublin, 6 further cases are reported, together with an account of methods for the detection of the accompanying deficiency of fibrinogen; the management of such cases is also discussed. Of the 6 cases described the condition was associated with concealed accidental haemorrhage in 2, with amniotic-fluid embolism in one, and with the retention of a macerated foetus in an Rh-immunized mother in one; the fifth case was one of missed abortion in an Rh-positive woman, while in the sixth no obvious obstetrical emergency was present, but the authors suggest the possibility of inhalation of vomitus with liberation of tissue thromboplastin as the probable mechanism.

Methods for the detection of the condition are outlined. If the deficiency of fibrinogen is complete the blood will be incoagulable: if it is marked there is prolongation of the whole-blood clotting time. Frequently, however, the deficiency of fibrinogen is not sufficient to cause prolongation of the whole-blood clotting time. Two simple procedures for the assay of fibrinogen are described [the original paper should be consulted for the details]. The first method is dependent on the addition of thrombin to a series of dilutions of the blood, the lowest dilution to give discernible fibrin formation providing the reading. In the second method the fibrin is collected after clotting with thrombin and estimated colorimetrically, using a biuret method. The instrument is calibrated by duplicate estimations made by the Kjeldahl technique.

In the management of patients with this condition the authors stress that dangerous bleeding may be provoked by active obstetrical intervention in cases in which no manifest bleeding has occurred. Administration of the fibrinogen fraction or dried plasma reconstituted in triple or quadruple strength is recommended for restoration of the coagulation defect. The transfusion of stored whole blood, which has a fibrinogen content of 200 mg. per 100 ml. or less, may not raise the fibrinogen concentration to a haemostatic level.

A. S. Douglas

412. **Blood Coagulation Failure in Obstetrics. Effects of Dextran and Plasma**

J. S. SCOTT. *British Medical Journal* [*Brit. med. J.*] **2**, 290–293, July 30, 1955. 2 figs., 20 refs.

A haemorrhagic condition occurring as a complication of certain obstetrical emergencies has been increasingly recognized in recent years [see Abstract 411]. In the present paper from the University of Liverpool the author discusses possible causes of the condition and points out that consideration of the available evidence suggests that the increased incidence during the last few years may be related to the increased use as "plasma expanders" of artificial macromolecular substances such as dextran. A possible mechanism is that the dextran exerts its effect by simple dilution of the already decreased fibrinogen concentration which follows haemorrhage and also by encouraging the precipitation of fibrinogen as fibrin or the formation of a dextran–fibrinogen compound which is precipitated.

In cases in which this disturbance of blood coagulation is likely to occur, such as in accidental antepartum haemorrhage, the author stresses that plasma should be given in place of dextran to increase the blood volume. Dried plasma reconstituted to double strength provides a readily available source of fibrinogen. It is probable that some deficiency of fibrinogen is often present in these obstetrical emergencies without being of such a degree as to cause haemorrhage, and in such cases the administration of dextran may be the precipitating factor which starts abnormal bleeding. Emphasizing the importance of a simple and rapid method for recognizing fibrinogen depletion the author states that the deficiency of fibrinogen can be detected by observing the clotting time of citrated blood on the addition of a standard solution of thrombin. *A. S. Douglas*

Respiratory System

413. **Drowning**
K. W. DONALD. *British Medical Journal* [*Brit. med. J.*] 2, 155–160, July 16, 1955. 22 refs.

Published experimental work on drowning, which is reviewed, shows that in dogs drowned in fresh water haemodilution is accompanied by haemolysis and an increase in the potassium:sodium ratio in the plasma; death is due to ventricular fibrillation, which usually occurs 3 to 7 minutes after submersion. Respiratory failure is almost simultaneous with the onset of ventricular fibrillation, but in some instances it occurs shortly before (10 to 20 seconds) and sometimes shortly afterwards (10 to 20 seconds). Haemodilution, haemolysis, electrolyte disturbances, and ventricular fibrillation are not observed in dogs drowned in salt water; the heart action fails gradually in 5 to 8 minutes. In both fresh- and salt-water drowning there is severe pulmonary oedema with plasma exudation into the alveoli causing tenacious froth in the air passages. Some workers have found that in dogs respiratory failure often occurs some time before circulatory failure begins; in such circumstances prompt administration of artificial respiration would almost certainly be successful.

The author emphasizes that resuscitation by artificial respiration must be started immediately the subject is taken from the water and should be continued for at least 15 minutes before any other procedures—examination of the patient, postural drainage, and administration of oxygen or drugs—are undertaken. The airway must be watched, but this should be attended to after artificial respiration has been started. Even if the subject is not responding in any way artificial respiration should be continued for at least an hour. The Holger Nielsen back-pressure–arm-lift method of artificial respiration is recommended. *A. I. Suchett-Kaye*

414. **An Electromyographic Examination of the Role of the Intercostal Muscles in Breathing in Man**
E. J. M. CAMPBELL. *Journal of Physiology* [*J. Physiol. (Lond.)*] **129**, 12–26, July 28, 1955. 7 figs., 13 refs.

The electrical activity of the intercostal muscles in 10 healthy male subjects and 4 patients with dyspnoea at rest was recorded at the Middlesex Hospital, London, using surface electrodes and, in one of the healthy subjects, concentric needle electrodes. Activity was detected in the lower intercostal muscles of both healthy and dyspnoeic subjects during inspiration and also during forced expiratory movements, but not during involuntary expiration, even with a considerable degree of hyperpnoea. Only with the needle electrode could some activity be detected towards the end of a maximum expiration at a rate of 50 to 60 litres a minute. The upper intercostal muscles were apparently much less active than the lower, which in turn were less active than the abdominal muscles during quiet respiration. Studies with the needle electrode did not reveal any difference in function between the external and internal intercostal muscles.

It is concluded that the intercostal muscles are inspiratory in function during involuntary breathing, but that they probably facilitate forced voluntary expiratory efforts such as coughing. *W. A. Briscoe*

415. **The Respiratory Function of the Laryngeal Muscles**
J. H. GREEN and E. NEIL. *Journal of Physiology* [*J. Physiol. (Lond.)*] **129**, 134–141, July 28, 1955. 7 figs., 5 refs.

Electromyographic studies were carried out at the Middlesex Hospital Medical School, London, on the intrinsic muscles of the larynx of anaesthetized cats, and records were made of the electrical activity in the recurrent laryngeal nerve.

Most of the activity in the recurrent laryngeal nerve occurred during inspiration. This activity could be abolished by inflation of the lungs, stimulation of the pulmonary stretch receptors presumably causing reflex inhibition of the discharge in the recurrent laryngeal nerve, the inhibition being abolished by section of both vagus nerves. The crico-arytenoideus posterior muscle, which widens the glottis, was electrically active during inspiration, and its activity was also abolished by inflation of the lungs. The crico-arytenoideus lateralis muscle, which contracts the glottis, was electrically active during expiration. *W. A. Briscoe*

416. **The Laboratory Background to the Use of Penicillin in Chronic Bronchitis and Bronchiectasis**
J. R. MAY. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 166–173, July, 1955. 2 figs., 13 refs.

This report deals with the results achieved with various preparations of penicillin in the treatment, at the Brompton Hospital, London, of 45 patients with chronic purulent bronchitis or bronchiectasis, none of whom was suffering an acute exacerbation. Three specimens of the patients' sputum were cultured for organisms before and after therapy, and the penicillin concentration in the sputum was determined at stated intervals. The preparations employed were crystalline benzylpenicillin, procaine penicillin, and "estopen", the hydriodide of the diethylaminoethyl ester of penicillin.

In 20 patients from whose sputum pneumococci were cultured all 3 types of penicillin therapy were effective in eliminating these organisms; but in 13 of these cases *Haemophilus influenzae* was cultured from the sputum after the course of penicillin. In the second group of 25 patients *H. influenzae* was present in the sputum before therapy began. In these patients only estopen, in doses of 500,000 units four times a day, was

effective. In this group smaller doses of estopen were ineffective, as were also crystalline benzylpenicillin (in doses up to 1 mega unit 4 times a day) and procaine penicillin. *P. Mestitz*

417. **The Late Results of the Conservation of the Apical Segment of the Lower Lobe in Resections for Bronchiectasis**

E. HOFFMAN. *Thorax* [*Thorax*] **10**, 137–141, June, 1955. 2 figs., 4 refs.

The author has reviewed the late results of basal segmental resection with conservation of the apical segment of the lower lobe in 51 cases of bronchiectasis treated at Shotley Bridge Hospital, Newcastle upon Tyne, and has compared them with those obtained in similar series of cases in which complete lobectomy, with and without resection of the lingula, was undertaken. After 6 months the results in the former group were poor as judged by bronchography, there being a high incidence of atelectasis of the residual apical segment, to account for which no common factor could be found. However, when the follow-up was continued over a longer period (2 to 6 years) it was found that many of the atelectatic segments eventually re-expanded, and that when they did so the bronchogram often returned to normal. Thus at 1 to 6 months atelectasis of the residual apical segment was present in 24 out of the 51 cases, whereas after 2 to 6 years it was found in only 4 of the 49 cases followed up. Bronchiectasis of the residual lung was present in none of these 49, whereas it was found in 3 out of 51 cases in which resection of the whole lower lobe and lingula had been carried out and in 1 out of 51 in which resection had been confined to the lower lobe.

On this evidence the author recommends that a conservative policy be adopted for several years when atelectasis of the residual segment occurs after partial lobectomy. *J. R. Belcher*

418. **The Treatment of Pulmonary Blastomycosis**

T. TAKARO, J. E. T. HOPKINS, and J. D. MURPHY. *Diseases of the Chest* [*Dis. Chest*] **28**, 203–216, Aug., 1955. 33 refs.

From the Veterans Administration Hospital, Oteen, N. Carolina, the results of various forms of treatment in 13 cases of blastomycosis, " the rarest and most lethal of the three common pulmonary mycotic infections ", are reported. Potassium iodide was given, either alone or together with some other form of treatment to 8 patients, of whom 4 are known to have died, 2 have recovered after subsequent treatment with other agents, and 2 who received no other drug remain clinically well but still carry the organisms in the sputum. Undecylenic acid was given in doses of 10 to 25 g. daily for an average of 40 weeks to 7 patients, 2 of whom had been treated originally with iodide: in one case, in which undecylenic acid was the only agent used, the pneumonic infiltration resolved completely, while in another case a systemic dissemination which followed pneumonectomy for a supposed carcinoma was cured with undecylenic acid after an initial failure with iodide; 3 of 5 patients who received surgical treatment or stilbamidine, or both, in addition were cured, and there was clinical improvement without complete cure in the other 2. Stilbamidine was given intravenously in doses of 150 mg. daily to 4 patients, who received an average of 6·8 g. in 2 or 3 courses; 3 of these patients had failed to respond to other forms of treatment given previously, and one was treated with undecylenic acid and stilbamidine in combination for a pneumonic lesion; marked clinical improvement was noted in 2 cases and some improvement in all 4. Surgical treatment included pneumonectomy (2 cases), lobectomy (2 cases), and decortication and unroofing of an abscess pocket, bilateral orchidectomy, and rib resection for drainage of a lung abscess each in one case.

The authors conclude that a completely satisfactory form of treatment for this disease has not yet been found, and that combined therapy with undecylenic acid and one of the diamidine derivatives is probably the best method of treatment available at the moment. They suggest that pulmonary resection may be useful for localized, stable lesions. *Kenneth Marsh*

419. **Surgical Treatment of Localized Emphysematous Disease**

W. WEISEL. *Annals of Surgery* [*Ann. Surg.*] **142**, 17–27, July, 1955. 18 figs., 16 refs.

Two primary clinical types of pulmonary emphysema are recognized—cystic and diffuse. In the former, which is the more common, the cysts take the form of blebs, bullae, or pneumatoceles; severe respiratory embarrassment may result from progressive distension of the lesions with compression of adjacent normal lung tissue, while rupture of a cyst may cause spontaneous pneumothorax or haemorrhage. In this paper from St. Joseph's and the Veterans Administration Hospitals, Milwaukee, 40 cases of cystic emphysema are reviewed. Of 17 patients who refused surgical treatment, 9 died from the disease, 6 became worse, and 2 were unchanged. On the other hand, of 23 patients subjected to operation, 22 were markedly improved and leading a normal life at the time of the report; the one death in this group was due to pulmonary embolism. The surgical treatment of choice was thoracotomy with conservative resection of the cysts, but in those cases in which the patient was considered unfit for thoracotomy good results were obtained by prolonged catheter drainage of the cysts. Clinical examination and respiratory function studies in these cases showed a return to normal after surgery; further, there was no evidence of recurrence or of progression of emphysema. The series included 4 newborn infants with localized tension cysts; all were treated by thoracotomy and local excision of the cysts and recovered without incident.

In 5 newborn infants with diffuse lobar emphysema bronchoscopy revealed abnormalities of the lobar bronchus; bronchoscopic dilatation was carried out in all 5 cases, with clinical and radiological improvement, although the final outcome remained uncertain.

The author considers that the importance of localized emphysema and the excellent results to be achieved by surgical treatment are not sufficiently appreciated.

F. J. Sambrook Gowar

420. **The Progress of Pulmonary Deficiency in Emphysema**

J. D. SINCLAIR. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **49**, 157–165, July, 1955. 1 fig., 15 refs.

In the study of 67 patients with emphysema here reported from Green Lane Hospital, Auckland, New Zealand, an attempt was made to correlate the clinical assessment of the dyspnoea with the progress of pulmonary deficiency as shown by the results of the determination of vital capacity, maximum breathing capacity, residual volume, functional residual volume, intrapulmonary gas mixing, and arterial oxygen saturation. The methods are described.

No single test was consistently satisfactory throughout the whole range of the disease process, and correlation between the results of the several tests was only fair. Diminution of the residual volume and functional residual volume were indicative of changes early in the disease, while reduction in vital capacity and maximum breathing capacity were correlated with later but more consistent changes. Of 13 of these patients in whom the tests showed pulmonary function to be worse than clinical examination had suggested, all fared badly in a short follow-up period of 18 months: 4 have died, 3 have had episodes of dangerous respiratory embarrassment, one showed signs of severe pulmonary hypertension, and one has developed congestive heart failure. On the other hand, of the patients in whom the tests showed reasonably good pulmonary function, none is known to have deteriorated. The author suggests that, over this limited period at least, the tests gave a more accurate prognosis than did clinical examination. *P. Mestitz*

421. **Etiological Diagnosis of Pleural Effusion by Pleural Biopsy**

M. J. SMALL and M. LANDMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 907–912, July 16, 1955. 5 figs., 18 refs.

The diagnosis of pleural effusion occurring in previously healthy young adults has always presented a problem since there are considerable differences in the ability of various laboratories to demonstrate, either bacteriologically or by guinea-pig inoculation, the presence of tubercle bacilli in pleural fluid. In this paper 5 cases are described in which, as the aetiology of the effusion could not be established by ordinary clinical and laboratory procedures, pleural biopsy was carried out, an oblong section of parietal pleura measuring approximately 1·5 by 3 cm. being removed for this purpose. The findings were surprising because of the advanced degree of infection of the pleura observed in all 5 cases. The authors state that this demonstration of multiple tubercles in the pleura of patients with tuberculous effusion would seem to indicate that direct pleural involvement in tuberculous pleural effusion is far more extensive than has hitherto been thought to be the case. The findings also cast doubt on the validity of previously accepted views on the aetiology of tuberculous effusion, especially the view that it is a manifestation of an allergic process. *D. P. McDonald*

422. **Bilateral Hilar Adenopathy: its Significance and Management**

C. H. HODGSON, A. M. OLSEN, and C. A. GOOD. *Annals of Internal Medicine* [*Ann. intern. Med.*] **43**, 83–99, July, 1955. 7 figs., 17 refs.

After a discussion of the diagnostic problems raised by the discovery of bilateral enlargement of the hilar lymph nodes on routine *x*-ray examination, with a brief review of the literature, the authors present an analysis of the records of a group of such cases from the Mayo Clinic. Only those cases were selected in which three examiners were unanimous that the stereoscopic films showed bilateral enlargement of the hilar nodes, and it is recognized that " they probably constitute only a small part of the cases of bilateral hilar adenopathy seen at the Mayo Clinic " during the 7-year period covered, and that " they cannot be analyzed statistically as a representative series ".

The cases are grouped as follows. (1) *Indeterminate disease.* This group contained 46 patients aged 16 to 64, 23 being males and 23 females. All were in good general health, but 13 had joint symptoms and 9 of these also had erythema nodosum. In 11 cases there was " parenchymal involvement of the lungs ". In 31 cases follow-up radiographs were available, and in only 7 of these had the adenopathy persisted, in one case for 8 years. Although no definite diagnosis was made, it is thought possible that many of these patients had sarcoidosis. (2) *Sarcoidosis.* In this group there were 44 patients aged 9 to 70, 18 being males and 26 females. Diagnosis was based on biopsy. Again all were in good general health, but 10 had joint symptoms and 3 had erythema nodosum. In 27 cases follow-up films were available and showed that the adenopathy might clear in less than 6 months or might persist for more than 6 years. Parenchymal lung involvement occurred in 12 cases. (3) *Lymphoma.* Of the 11 cases in this group, 9 were derived from a survey of 100 consecutive cases of histologically proven lymphoma of various types. The *x*-ray appearances were in most cases indistinguishable from those in the first two groups. However, all the patients were ill and all had other enlarged lymph nodes or skin lesions available for biopsy, while none had joint symptoms or erythema nodosum. (In a survey of 100 consecutive cases of leukaemia no instances of hilar adenopathy were found.) (4) *Metastatic malignant tumours.* In the 6 patients in this group the *x*-ray appearances were similar to those in the other groups. None of the patients had joint symptoms or erythema nodosum. (5) *Miscellaneous.* This group contained one case each of bacteriologically proven tuberculosis, silicosis, and fibrocystic disease of the pancreas.

The authors conclude that since rapid regression of enlarged hilar lymph nodes occurs so frequently in the benign conditions, similar regression following *x*-ray therapy cannot be regarded as diagnostic of a reticulosis and it is suggested that *x*-ray therapy should be used only for histologically proven malignant disease. They also conclude that when bilateral hilar lymphadenopathy is accompanied by erythema nodosum it is unlikely to be due to a malignant disease. *C. M. Fletcher*

Urogenital System

423. **Electron-microscopical Studies of the Structure of the Renal Glomerulus in Mammals.** (Recherches au microscope électronique sur la structure du glomérule rénal des mammifères)
A. POLICARD, A. COLLET, and L. GILTAIRE-RALYTE. *Archives d'anatomie microscopique et de morphologie expérimentale* [*Arch. Anat. micr.*] **44**, 1–19, 1955. 12 figs.

The kidneys of adult white rats were fixed in 2% osmic acid buffered to *p*H 7·5, embedded in butyl methacrylate, and sections 0·1 μ in thickness cut and studied with the electron microscope.

The authors confirm the presence of a " mesangium " which supports the capillary loops of the glomerulus; it contains nuclei and dense cytoplasm, and often has a fibrillar appearance. They state that the basement membrane of the capillaries is homogeneous and does not give off processes such as have been described by earlier authors. With high magnification it can be seen that such processes are actually derived from the cells of the covering epithelium (Bowman's cells) so that these cells may be described as being applied to the basement membrane by a number of " feet " which are separated by lacunae. The soles of the " feet " are separated from the basement membrane by a narrow space (150 Å) which is transversely striated. The lacunar spaces form a network of fine canals which lie between the capillary basement membrane and the covering epithelium and which communicate with spaces between the epithelial cells themselves. The epithelial cells have a large nucleus with a dense nucleolus. The cytoplasm is finely reticulated and contains vacuoles which are apparently empty. *D. B. Moffat*

424. **The Effect of Hyaluronidase on Renal Glomerular Function in Normal Subjects and in Patients with Kidney Disease.** (Influenza della jaluronidasi sulla funzionalità renale glomerulare in soggetti normali e nefropatici
A. BERGAMINI, G. SCAPINELLI, and G. BENATTI. *Minerva medica* [*Minerva med. (Torino)*] 2, 527–532, Sept. 8, 1955. 1 fig., 39 refs.

In an experimental study carried out at the University Medical Clinic, Modena, the authors attempted to increase the glomerular filtration rate (G.F.R.) in 7 patients without obvious renal disease and in 5 with focal glomerulonephritis, 3 with diffuse glomerulonephritis, and 2 showing signs of nephrosis, by the injection of from 250 to 2,500 units of hyaluronidase, in 6 cases intramuscularly and in 11 intravenously. Various tests of renal function were carried out before and after the experiment.

Hyaluronidase given by intramuscular injection produced no measurable change in the G.F.R. in any of the patients. After intravenous injection, however, the G.F.R. rose by up to 25% in the controls and nephritic patients; but in 3 of those suffering from glomerulonephritis and in the 2 cases of nephrosis there was a comparable fall in the G.F.R., a result which the authors ascribe to the complexity of the chemical changes involved. *L. Michaelis*

425. **Correlation between Renal Function and Histology**
A. E. PARRISH, N. H. RUBENSTEIN, and J. S. HOWE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 632–637, June, 1955. 7 figs., 7 refs.

It has been stated that the degree of renal dysfunction shown by renal function tests does not always accurately reflect the extent of pathological change in the kidney. In a study at George Washington School of Medicine, Washington, D.C., glomerular function was estimated in 25 patients with various renal disorders by inulin clearance, and maximum tubular excretory capacity by clearance of PAH. Two or three days later renal biopsy was performed with a Turkel needle; in studying the biopsy material special attention was paid to grading the pathological changes in the glomeruli and tubules.

The results showed that there was a rough correlation between the degree of glomerular damage as determined by histological examination and reduction of inulin clearance and also between tubular atrophy or epithelial damage and PAH clearance, the correlation being best in cases of glomerular nephritis. Minor abnormalities of the glomeruli seemed more likely to affect renal function than minor changes (such as epithelial vacuolization) in the tubules. *K. G. Lowe*

426. **Treatment of the Nephrotic Syndrome with Corticotropin (ACTH) and Cortisone. A Four-and-one-half-year Survey of Results with Short-term Courses**
W. HEYMANN, S. SPECTOR, L. W. MATTHEWS, and D. J. SHAPIRO. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 22–27, July, 1955. 13 refs.

The results obtained with short-term courses of corticotrophin (ACTH) or cortisone in 64 children aged 1 to 9 years with the nephrotic syndrome are reported. No significant difference between the effects of the two drugs was noted. An over-all incidence of diuresis of approximately 80% in 153 courses of ACTH or cortisone was obtained, diuresis occurring rather more frequently during administration of the drug than after withdrawal. The incidence of diuresis was lower in children in whom the disease later progressed to renal failure, even although there was no indication at the time of progressive renal disease. No attempt was made to distinguish cases of pure nephrosis from those of nephrotic nephritis, but patients with fixed azotemia or persistent hypertension were excluded.

Of the 64 children, 43 required only three courses of treatment, the total stay in hospital of these being 1 to 1½ months. However, although morbidity was much reduced by administration of these drugs, the mortality rate was not significantly improved; 17 patients died, 14 of them in renal failure. *Margaret D. Baber*

Endocrinology

427. **Assessment of Adrenocortical Function in Cases of Pituitary Tumour**
H. J. CROW. *British Medical Journal* [*Brit. med. J.*] **2**, 401–405, Aug. 13, 1955. 12 refs.

In this paper from the Neurosurgical Unit and the Royal Infirmary, Bristol, the author describes briefly the clinical endocrine status, with special reference to the pituitary–adrenal system, of 18 patients with benign pituitary tumour who later came to operation, the indication for operation in each case being progressive visual loss. An attempt was made to supplement this assessment by a glucose tolerance test and the diuresis test of Robinson *et al.* (*Proc. Mayo Clin.*, 1941, **16**, 577). Fractional test meals were also carried out in the majority of the patients in view of the reported frequency with which relative or complete achlorhydria is found in hypopituitarism.

In 6 patients there was sufficient evidence of adrenocortical insufficiency to call for preoperative administration of corticotrophin. This was followed by improvement in the clinical state and in the results of the biochemical tests. Only one of the 5 patients who survived operation in this group had an endocrine disturbance—an Addisonian-like crisis resulting from the premature withdrawal of corticotrophin.

Of the 12 patients who did not have corticotrophin before operation, 2 in whom, on the author's assessment, there was no significant impairment of pituitary–adrenocortical function and one in whom such impairment was slight developed crises after operation which required hormone treatment.

From the literature and from personal experience the author concludes that the states of torpor and of crisis which may follow pituitary operations are—except possibly for some slight modifications due to frontal-lobe damage—identical with the syndrome of " hypopituitary coma " occurring in cases of chronic hypopituitarism.

H.-J. B. Galbraith

428. **Use of Thyroid Hormone to Differentiate between Hyperthyroidism and Euthyroidism**
M. PERLMUTTER and S. SLATER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 718–720, July 2, 1955. 1 fig., 13 refs.

In this study of the diagnostic value of thyroid hormone, carried out at the Maimonides Hospital of Brooklyn, New York, 96 patients with diseases unrelated to the thyroid gland together with 33 patients suspected of having hyperthyroidism or nodular goitre were given 20 to 40 μc. of radioactive iodine (^{131}I) in water without added sodium iodide, the uptake of ^{131}I being measured 24 hours later by a bismuth-tube Geiger counter. The patients then received either thyroid extract (260 mg. per day) for 2 weeks, or triiodothyronine (35 to 75 mg. daily) for 1 to 2 weeks. Immediately before the ingestion of a second tracer dose of ^{131}I the radiation from the thyroid area was again measured. Since 9% of ^{131}I disappears in 24 hours, 91% of the retained radioactivity from the first dose was subtracted from the thyroid radioactivity recorded 24 hours after the ingestion of the second tracer dose. To minimize the error in calculation of the retained radioactivity, the second dose was usually larger than the first.

In 108 of the 129 subjects tested the initial uptake was at least 40% of the ingested dose of ^{131}I. A decrease of more than 30% in the initial iodine uptake was noted in 3% of the hyperthyroid patients and in 95% of the euthyroid patients. The authors suggest that this test would help to differentiate cases of hyperthyroidism from euthyroid cases. They note, however, that the value of the test is limited by the observation that in about half the patients with hyperactive, non-toxic, solitary nodular goitre inhibition of the active nodule failed to occur.

Norval Taylor

ADRENAL GLANDS

429. **Hermaphroditism, Gender and Precocity in Hyperadrenocorticism: Psychologic Findings**
J. MONEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 253–264, June, 1955. 1 fig., 5 refs.

Sixty infants, children and adults, representing 7 types of hermaphroditism and including 39 hyperadrenocortical females, have been under comprehensive psychologic investigation. Gender role and outlook as boy or man, girl or woman, was found to be in agreement with sex of rearing, except in 3 cases, and not to be automatically or instinctively determined by chromosomes, gonads or hormones. Twelve hyperadrenocortical females and 10 males were under study while still precociously virilizing. In psychological maturity, they resembled children of their age, though precocious physique, when combined with high IQ, permitted acceleration of psychological development in some respects, if life experiences also promoted it.—[Author's summary.]

430. **Hermaphroditic Genital Appearance, Rearing and Eroticism in Hyperadrenocorticism**
J. G. HAMPSON. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **96**, 265–273, June, 1955. 1 fig., 2 refs.

External genital morphology agreed with assigned sex in over half of the 60 hermaphroditic individuals studied; it was therefore a salient determinant of the experiences they encountered from the day of birth onward and, subsequently, of the life experiences they transacted. Among the 22 who lived with a contradiction between

external genital morphology and assigned sex, 21 had a gender role and erotic practices wholly consistent with assigned sex and rearing. Prompt and unequivocating decision of the sex of assignment was found beneficial, along with early reconstructive genital surgery, as required. Reassignment or change of sex in childhood, with or without genital surgery, was found to constitute an extreme psychologic hazard. Physically precocious children presented no untoward social problems of sexual misconduct.—[Author's summary.]

431. **Metabolic, Functional, and Clinical Aspects of Treatment with "Deltacortene" [Prednisone].** (Alcuni aspetti metabolici, funzionali e clinici registrati in corso di terapia con deltacortene)

B. BONATI, A. BERGAMINI, G. B. RANCATI, and G. F. TEDESCHI. *Minerva medica* [*Minerva med. (Torino)*] 2, 26–33, July 4, 1955. 5 figs., 24 refs.

At the Institute of Clinical Medicine and Therapeutics of the University of Modena 8 patients with a variety of conditions were treated with prednisone ("deltacortene") and its effects carefully evaluated. The cases included 1 of adrenal virilism, 2 of rheumatoid arthritis, 1 of ankylosing spondylitis, 3 of bronchial asthma, and 1 of lupus erythematodes with arthritis. The drug was given by mouth in 3 or 4 doses daily, the total dosage on the first day being 35 mg., followed by 30 mg. for 3 days, 20 mg. for 3 days, 15 mg. for 4 days, and 10 mg. thereafter. The period of treatment ranged from 10 to 35 days. A dosage of less than 10 mg. daily did not appear to be effective.

Clinically, the results of treatment were satisfactory in all cases and much superior to those obtained with cortisone—for example, the patient with adrenal virilism started menstruating after 12 days compared with 45 days with cortisone in doses three times greater. One of the patients with asthma, who had an active duodenal ulcer in addition, was able to continue treatment with prednisone, whereas the administration of ACTH or cortisone had caused severe epigastric pain and had had to be discontinued. The drug's marked diuretic effect was confirmed; it was noticeable in the first 4 to 6 days of treatment and was accompanied by increased urinary excretion of chlorides. No other side-effects were observed.

Laboratory investigation of the endocrine effects showed that after 7 days there was a considerable reduction in the urinary excretion of 17-ketosteroid and a modest increase in that of 11-oxycorticoids; the urinary excretion of gonadotrophins was unchanged. Studies of renal function indicated that there was an increase in glomerular filtration and a decrease in tubular reabsorption of water. Blood coagulation was not affected. After 15 days' treatment the serum globulin content had become normal in one patient with rheumatoid arthritis, and an increase in the serum cholesterol level was noted in 6 other patients.

The effects of prednisone on the urinary steroid and gonadotrophin excretion suggest that it acts in part by a suppressive effect on the anterior lobe of the pituitary gland. *V. C. Medvei*

432. **The Metabolic Effects of "Metacortandracin" [Prednisone] and 9-α-Fluorohydrocortisone Acetate.** (Effetti metabolici del metacortandracin e del 9-α-fluoroidrocortisone acetato)

G. SALA, G. D'AMICO, E. PASARGIKLIAN, A. AMIRA, and C. B. BALLABIO. *Reumatismo* [*Reumatismo*] 7, 127–137, May–June, 1955. 10 figs., 24 refs.

9-α-Fluorohydrocortisone causes an increase of the body fluids (intra- and extracellular) with retention of water, chlorides, and sodium and increased potassium excretion (Na:K being increased). [Incomplete] studies of the carbohydrate metabolism seem to show a diminished sensitivity to insulin. The blood eosinophil count shows no definite change. The excretion of urinary 17-ketosteroids is much diminished. The adrenal function is depressed, even after only short treatment.

Prednisone produces an increase in the urinary sodium excretion and diuresis without obvious alteration of the plasma electrolytes. The effect on carbohydrate metabolism is not convincing, but perhaps slightly diabetogenic. The eosinophil count is diminished and urinary 17-ketosteroid excretion decreased. There is little influence on the excretion of uric acid in gouty subjects, although clinically the result was equal to that of phenylbutazone and was excellent in one case. Adrenal function is depressed.

There does not seem to be any causal relation in the case of either steroid between its influence on the mineral and carbohydrate metabolism and its effect on the signs of inflammation and its antiphlogistic action.

V. C. Medvei

433. **Effect of 9α-Fluorohydrocortisone on Adrenal Hyperfunction in Cushing's Syndrome**

C. L. COPE and R. J. HARRISON. *British Medical Journal* [*Brit. med. J.*] 2, 457–460, Aug. 20, 1955. 3 figs., 11 refs.

9-α-Fluorohydrocortisone has been reported to have twenty times the therapeutic potency of cortisone and about one-tenth of the sodium-retaining power of aldosterone, and has been shown to have an inhibitory effect on the normal adrenal cortex. Because the breakdown products of cortisone and hydrocortisone are essentially like those occurring naturally in the urine and plasma, it is impossible to assess the inhibitory effect of cortisone on the normal or hyperplastic adrenal cortex by determination of the excreted adrenal steroids; this, however, does not hold for 9-α-fluorohydrocortisone, the breakdown products of which are different from those derived from hydrocortisone. Taking advantage of this fact the authors have observed the inhibitory effect of 9-α-fluorohydrocortisone in a typical case of Cushing's syndrome, in which the diagnosis was later confirmed by laparotomy. Adrenal function was assessed by the measurement of the daily excretion of 17-ketosteroids, 17-ketogenic steroids, and hydrocortisone. They found that on administration by mouth of a daily dose of 5 mg. of 9-α-fluorohydrocortisone (equivalent to about 100 mg. of cortisone) hydrocortisone excretion was reduced by 50%, and with a dose of 15 mg. daily by 80%. The output of hydrocortisone returned to its previous high level when the drug was withdrawn. The excre-

tion of 17-ketosteroids and ketogenic steroids was uninfluenced.

From all available evidence it appeared likely that the new steroid had suppressed the production of hydrocortisone by the adrenal cortex. It is considered that this action is probably analogous to that of cortisone in the adrenogenital syndrome, in which cortisone suppresses excessive ketosteroid excretion if this is due to hyperplasia, but not if it is due to tumour formation. By the use of 9-α-fluorohydrocortisone it might, therefore, be possible to differentiate between Cushing's disease due to cortical hyperplasia—as was probably the case in the patient studied—and that due to tumour.

The authors conclude that the inhibitory effect of this steroid is mediated through the pituitary gland by a sudden increase in the plasma concentration of hydrocortisone-like substances. *J. N. Harris-Jones*

434. **Sodium Retention and Edema from Percutaneous Absorption of Fludrocortisone Acetate**
T. B. FITZPATRICK, H. C. GRISWOLD, and J. H. HICKS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 1149–1152, July 30, 1955. 3 refs.

In a number of trials of the therapeutic effect of the topical application of hydrocortisone in cases of dermatitis the authors observed improvement not only in treated areas, but also in control areas. Systemic absorption of the hormone was thought to be responsible, but there was no increase in the urinary excretion of hydrocortisone in 2 patients with generalized dermatitis who were treated with 100 ml. of 2·5% hydrocortisone lotion daily for 7 days.

More striking clinical evidence of systemic absorption was noted, however, in later trials of topically applied 9-α-fluorohydrocortisone acetate. In addition, in 5 patients treated with lotions containing fluorohydrocortisone to a total daily dosage of 15 to 30 mg. oedema developed, and in 8 treated with lotions or ointments containing from 0·1 to 0·25% of fluorohydrocortisone there was a gain in weight of over 5 lb. (2·27 kg.) within a week of the start of treatment.

In a further series of 7 patients with various dermatological disorders fluorohydrocortisone ointment or lotion was applied 3 times a day and the urinary excretion of sodium determined. In all 7 patients there was a reduction in urinary excretion of sodium during the first 2 or 3 days of treatment. In 3 a marked reduction in urinary output was observed and in 3 there was a gain in weight of 5 lb. After the initial period of sodium and water retention an increase in sodium excretion occurred, coincident with improvement in the dermatitis. In at least one of the patients in whom oedema developed the swelling became less while treatment with fluorohydrocortisone continued; it is suggested that the absorption of the hormone decreased as the dermatitis improved. In 3 other patients there appeared to be little change in the serum sodium, potassium, or chloride levels during a 3-day period of topical application of fluorohydrocortisone.

The authors suggest that sodium retention and oedema are more likely to occur when (1) the hormone is applied in high concentration or with excessive frequency, (2) the dermatitis is in an acute phase, (3) the treated area—for example, the perineum—is naturally moist, (4) the preparation is massaged into, rather than lightly applied to, the skin, and (5) a lotion rather than an ointment vehicle is used. *H.-J. B. Galbraith*

435. **Metabolic Studies with Aldosterone in a Patient with Addison's Disease and in a Normal Subject**
S. I. GRIBOFF, R. WIENER, J. EISENBERG, A. IANNACCONE, and L. J. SOFFER. *Metabolism* [*Metabolism*] **4**, 289–294, July, 1955. 2 figs., 13 refs.

The metabolic effect of aldosterone was studied in a patient with Addison's disease and a healthy subject at the Mount Sinai Hospital, New York. The patient with Addison's disease had been well maintained on other hormone treatment, which, however, was withheld for 12 weeks before the present trial started. Aldosterone was given by intramuscular injection in a dosage of 100 μg. daily for 9 days to the patient and 200 μg. daily for 8 days to the control. Both received 500 mg. of sodium in the diet, with an additional daily supplement of 5 g. of sodium chloride by mouth. Metabolic studies included estimation of the sodium, chloride, and potassium balances and urinary excretion of neutral 17-ketosteroids, the carbohydrate tolerance, and response to water loading; blood pressure and the peripheral eosinophil count were also determined. There was retention of sodium and chloride in both subjects during administration of aldosterone; some potassium diuresis occurred in the patient with Addison's disease, but the healthy subject remained in positive potassium balance. Other findings indicated that Addison's disease was satisfactorily controlled by the hormone. With the small dosage employed no change in blood pressure, glucose tolerance curve, or response to the water-load test was noted in either the patient or the control subject. Moreover, the patient with Addison's disease was maintained in metabolic equilibrium through a moderately severe infection of the upper respiratory tract.
G. S. Crockett

436. **Increased Excretion of Aldosterone Immediately after Operation**
J. G. LLAURADO. *Lancet* [*Lancet*] **1**, 1295–1299, June 25, 1955. 2 figs., 41 refs.

It is well known that surgical trauma is followed by a positive sodium balance and a negative potassium balance, and it has been postulated that the recently isolated corticoid aldosterone (electrocortin) is responsible for this alteration in electrolyte metabolism. In the present paper from the University of Otago, New Zealand, the author reports the results of assay of aldosterone in the urine before and immediately after surgical operations on 6 adult patients with various disorders. The urinary excretion of sodium and potassium was determined by flame photometry at the same time. The author's methods for the extraction and bio-assay of aldosterone have been described in a previous paper (*Brit. med. J.*, 1954, **1**, 1290). Both the techniques were tested on pure crystalline aldosterone; the potency of

new steroid was found to be about 100 times that of deoxycortone acetate, and the amount recovered from human urine was about 20%.

Aldosterone was found in the urine of some of the patients during the 24 hours before operation, but not of all. In all 6 cases studied, however, there was a significant increase in sodium-retaining activity in the urine immediately after operation, corresponding to an aldosterone output ranging from 0·14 to 2·70 g. The increase closely paralleled a rise in urinary potassium and a fall in urinary sodium excretion. This correspondence between the change in the sodium : potassium ratio (determined chemically) and the sodium-retaining activity (determined biologically) points to a relationship between these two variables. It is probable that the sodium-retaining factor is aldosterone, since this compound has been isolated chromatographically from the urine of patients with similar electrolyte disturbances. Corticotrophin is not the specific stimulus for aldosterone, but there is some evidence of a relationship between this factor and the pituitary growth hormone.

Nancy Gough

DIABETES MELLITUS

437. **Insulin Zinc Suspension in Childhood Diabetes**
O. H. Wolff and T. G. Maddison. *British Medical Journal* [*Brit. med. J.*] **2**, 413–415, Aug. 13, 1955. 20 refs.

At the Children's Hospital, Birmingham, the authors have treated 20 children with typical juvenile diabetes with insulin zinc suspension (I.Z.S.)—a mixture of I.Z.S. (amorphous) and I.Z.S. (crystalline) in the proportion of 3 to 7—for periods of 5 to 13 months. Half of these were newly diagnosed cases, but the other 10 had been under treatment for 2 to 7 years; all but 2 were admitted to hospital for the change to the new insulin and remained there until stabilized, the remaining 2 being changed to I.Z.S. as out-patients.

On the average it required 3 weeks after the change before the urine passed before meals became free from sugar. When this was achieved blood samples for determination of sugar levels were taken 2-hourly by day and 4-hourly by night for 24 hours to check the adequacy of control; only minor alterations in the diet and dosage of insulin were found necessary. The degree of control in the out-patients was assessed by determining the total sugar content of a 24-hour collection of urine. The patients were considered to be in good control if they were free of symptoms, in good health, gaining weight, and passing less than 10 g. of sugar in 24 hours. All but 2, who are described in further detail, were judged to be in such control. The I.Z.S. was given in a single daily injection; the smallest dose was 20 units and the largest 92 units, 6 patients requiring more than 48 units. In 9 cases the dose had to be raised after the patient left hospital, in 4 by more than 10 units.

The 2 cases of failure aforementioned were in a 12-year-old girl with petit mal who had attacks when her urine was sugar-free, and in a boy of 9 who remained in good control while in hospital, but not after discharge when, it was thought, parental supervision of his diet was poor. In these 2 cases there was no reason to believe that the use of I.Z.S. (amorphous) or I.Z.S. (crystalline) would have led to better control. On the whole there were few hypoglycaemic reactions and only one episode, in one of the failed cases, gave rise to anxiety. The occurrence of low blood sugar levels without symptoms is attributed to the remarkably even hypoglycaemic action of I.Z.S.; no local reactions were encountered. The patients' diet was adjusted so that the ratio of total carbohydrate intake at breakfast, mid-morning snack, and midday dinner to that later in the day was 3 to 2. It is thought that this arrangement may account for the good results obtained without recourse to the other mixtures of amorphous and crystalline I.Z.S. The intakes of protein and fat were not measured. (In an addendum a further 8 cases which have been well controlled with I.Z.S. in hospital are mentioned.)

[It is of interest that the authors have not so far encountered a young patient in whom I.Z.S. has failed to control hyperglycaemia and to prevent ketosis, as have many workers in adult diabetes. One reason for this may be that their series is small.]

A. Gordon Beckett

438. **The Octogenarian Diabetic. Observations in Cases of Diabetes before and after the Age of Eighty Years**
H. F. Root and P. Barclay. *Diabetes* [*Diabetes*] **4**, 191–196, May–June, 1955. 3 refs.

In 0·5% of a large series of cases of diabetes seen at the Joslin Clinic and New England Deaconess Hospital, Boston, between 1939 and 1947, the onset of the disease occurred at age 80 or over. A review of 4,690 hospital admissions for diabetes in the 2 years 1952–53 revealed that 447 of the patients were between 70 and 91 years of age on admission, females outnumbering males by 2 to 1. The age at onset in these 447 patients showed a peak in the fifties, but 116 were 70 years or more at the onset. The average duration of the disease at the time of admission was 12·5 years. Although it is generally true that diabetes in the elderly is mild (none of the 447 patients was in diabetic coma), the insulin requirement in this series was often high (50 to 99 units daily); only 5·8% needed no insulin on discharge. Cerebral arteriosclerosis was diagnosed in 19·9%, arteriosclerotic heart disease in 52·1%, and peripheral vascular disease in 29·9%. Retinitis was noted in 22·6%, mostly when the diabetes was poorly controlled. Operation was performed in 102 cases, amputation being necessary in 51 of these. The serious problem presented, both to patients and to hospital management, by crippling foot lesions in elderly diabetics is emphasized. Careful and continuous control of the disease from the onset will prevent, or at least postpone, these sequelae, a modified diet with added protein being of special help in the elderly. The authors report one series of 20 patients (10 males and 10 females) who attained the age of 80 or more after having had diabetes for at least 35 years. In all these cases there had been strict control of diet from the onset of symptoms.

J. N. Agate

The Rheumatic Diseases

439. **Investigation of the Properties of a Substance with the Characteristics of a Tissue-specific Antibody Occurring in the Serum in Cases of Polyarthritis and Rheumatic Endocarditis.** (Untersuchungen über die Eigenschaften einer im Serum von Polyarthritikern und von Patienten mit rheumatischer Endocarditis vorkommenden Substanz mit den Merkmalen eines gewebsspezifischen Antikörpers)

C. STEFFEN and H. SCHINDLER. *Schweizerische Zeitschrift für allgemeine Pathologie und Bakteriologie* [*Schweiz. Z. allg. Path. Bakt.*] **18**, 287–302, 1955. 25 refs.

Working in the clinical laboratories of the Hanusch Hospital, Vienna, the first-named author, employing an anti-human-globulin (A.H.G.) deviation technique, has shown that the serum of patients suffering from rheumatoid arthritis and rheumatic endocarditis contains a substance with specific properties against cells of the heart, muscle, and joint capsules. Serum from healthy individuals and from patients suffering from diseases such as tuberculosis and pneumonia did not contain this substance, while the latter had no effect on cells of the spleen or liver. It was concluded that the substance was of the nature of an incomplete antibody with a specific activity against fibro-muscular tissue. In the further studies here reported its properties were investigated by a deviation technique (using Coombs serum) and by elution. [For details of the procedures the original should be consulted.]

Samples of serum from 13 patients with cardiac disease were incubated with cardiac tissue and mixed substrate; with 8 of these, from patients with active rheumatic endocarditis, definite A.H.G.-deviation was obtained, but 4 tests against muscle substrate gave no deviation. In one case, which ultimately proved fatal, it was actually found possible to use ante-mortem serum against the patient's own tissues. In 2 cases it was shown that the level of circulating antibody decreased with clinical improvement. Of samples of serum from 5 patients with cardiac disease who acted as controls, 4 showed no deviation with muscle, heart, and mixed substrate, while the fifth revealed antibody activity against muscle and mixed substrate but not against heart substrate.

Sera from 8 patients with rheumatoid arthritis were next examined, sera from 5 patients with neurasthenia and neuralgia being tested as controls. The former showed the presence of an antibody with specific action against muscle cells and mixed cells (from muscle, joint-capsules, and heart); 4 of these sera showed no specificity towards heart cells, but the remaining 4 revealed some specificity and inquiry showed that 3 of these patients had old cardiac damage. The 5 control cases yielded negative results. Absorption and elution techniques gave comparable results. *David Preiskel*

See also Endocrinology, Abstract 432.

RHEUMATIC FEVER

440. **Rheumatic Fever Activity Determination by Two Correlative Methods**

R. K. SKILLMAN, W. SPURRIER, I. A. FRIEDMAN, and S. O. SCHWARTZ. *Archives of Internal Medicine* [*Arch. intern. Med.*] **96**, 51–60, July, 1955. 25 refs.

At the Hektoen Institute for Medical Research (Cook County Hospital), Chicago, the authors investigated the value of two antigen–antibody reactions as a means of determining activity in rheumatic fever; the trial was carried out on 78 patients with rheumatic fever (active and inactive) and 77 controls. In Method I the serum of patients with rheumatic fever was used as antibody and sheep erythrocytes coated with heat-killed Group-A β-haemolytic streptococci from cases of rheumatic fever as the antigen, complement being then added to produce haemolysis. In Method II Group-A β-haemolytic streptococcus antiserum from immunized rabbits was employed as antibody and the patient's erythrocytes as antigen.

Method I, using the patient's serum as the antigen source, was found to be the more sensitive and showed better correlation with the clinical state. Of the patients in whom the disease was clinically active, 98% gave a positive haemolytic reaction, as against 89% with the agglutination method. In those in whom the disease was considered to be inactive the corresponding proportions were 48 and 30%. The height of the titre did not indicate the severity of the process, and showed no correlation with the erythrocyte sedimentation rate. Treatment with cortisone or salicylates did not interfere with the determinations. In all the 77 control subjects the reactions were negative by both methods.

It is concluded that these reactions are of practical value in assessing the activity of rheumatic fever, as well as in its diagnosis. *G. W. Csonka*

441. **The Clot Density Determination of Fibrinogen in Rheumatic Fever**

S. LOSNER, B. W. VOLK, and A. KANOF. *American Heart Journal* [*Amer. Heart J.*] **50**, 100–111, July, 1955. 7 figs., 28 refs.

In 33 cases of rheumatic fever and 6 cases of rheumatic heart disease without active rheumatism studied at the Jewish Chronic Disease Hospital, Brooklyn, New York, the plasma fibrinogen level was estimated at frequent intervals and compared with the erythrocyte sedimentation rate (E.S.R.). The latter was determined by Wintrobe's method, and the former by the spectrophotometric measurement of the increase in optical density of the plasma during clotting. In addition, tests for the presence of C-reactive protein (C.R.P.) were carried out at least once in every case.

An increase in the plasma fibrinogen level was found only when there was clinical evidence of active rheumatism, and was sustained only in cases with a protracted clinical course. The level remained normal in cases in which an elevated E.S.R. was unaccompanied by other evidence of activity and in cases of inactive rheumatic heart disease complicated by respiratory infection. If the level was increased initially, it fell rapidly when cortisone was given, often becoming abnormally low. In those cases in which cessation of hormone treatment was followed by a " rebound " of clinical activity the plasma fibrinogen level often rose transiently, this rise being preceded by an increase in E.S.R. and re-appearance of C.R.P. In general, the plasma fibrinogen level returned to normal before C.R.P. disappeared and long before the E.S.R. fell to normal, and the authors suggest that such a fall is a reliable indicator of a recession of the inflammatory process rather than of its complete subsidence.

S. C. Milazzo

442. **Rheumatic Heart Disease as a Problem of Preventive Cardiology**

G. Björck. *Journal of Chronic Diseases* [*J. chron. Dis.*] 1, 591–600, June, 1955. 1 fig., 8 refs.

A follow-up study was carried out during 1953 on 1,540 patients out of about 4,000 who had been admitted to Malmo General Hospital, Sweden, with rheumatic fever or some other manifestation of acute rheumatism, heart disease of presumed rheumatic origin, acute nephritis, or congenital heart disease during the years 1930–50. An analysis of data derived from these patients and from the records of about 500 others who had died in the meantime was made in an attempt to throw light on the natural history of rheumatic heart disease and the possibility of its prevention.

Of the 467 cases in which a definite diagnosis of rheumatic fever had been made originally, valvular disease was present at the time of follow-up in 25%; of 227 in which a diagnosis of " rheumatic fever (uncertain) " had been made, valvular disease was present in 11%; and of 51 patients with the original diagnosis of chorea (with no other rheumatic manifestation), 33% had valvular disease. Among the 120 cases of erythema nodosum and 311 of acute nephritis studied the incidence of heart disease was so low that it is concluded that in these conditions no prophylactic measures against its development are necessary. There was a high incidence of recurrence among the patients with definite rheumatic fever and chorea, and the higher incidence of heart disease in patients who had had several attacks clearly indicated the need for prophylaxis against recurrence. The first attack was by no means confined to childhood, as in 124 out of 467 cases of definite rheumatic fever it had occurred when the patient was between 20 and 29 years. There was a higher incidence of valvular disease in general in females than in males, although pure aortic lesions were far commoner in males than females.

It is suggested that there are four strategic points on which the attack on rheumatic heart disease should be concentrated: (1) adequate treatment of the first attack of acute rheumatism; (2) the prevention of recurrences; (3) the medical control and supervision of patients with " possible " and " potential " heart disease; and (4) the recognition of the correct time for surgical treatment.

[This paper contains much valuable statistical information which is difficult to abstract.]

C. Bruce Perry

443. **The Treatment of Acute Rheumatic Carditis with Prednisone.** (La terapia delle carditi reumatiche evolutive con Prednisone)

G. Casolo, A. Di Nardo, C. A. Maggi, L. Orcese, A. Zanazzi, and D. Ciafaloni. *Minerva medica* [*Minerva med. (Torino)*] **2**, 33–47, July 4, 1955. 12 figs., 16 refs.

Prednisone (" metacortandracin ") was used at the Ospedale Maggiore, Milan, in the treatment of 15 patients [ages not stated] with well-defined rheumatic carditis, which was classified as " acute " in 10 cases and " subacute " in 5. Severe cardiac decompensation was present in 3 of the acute cases and pancarditis in one. Antibiotic and cortisone treatment had been unsuccessful and in some cases had even aggravated the carditis. The prednisone was given by mouth 3 or 4 times daily in a total daily dosage of 30 to 40 mg. (except in 2 cases in which 50 mg. was given). The treatment was continued until the clinical and laboratory findings were normal or near normal, which occurred after 8 to 15 days' treatment in all but 3 cases in which progress was delayed and treatment carried on for 30 to 40 days.

All the patients responded well, and the more acute the condition, the greater was the therapeutic effect. The fact that the drug was so well tolerated permitted the use of large doses in two special circumstances: (1) in controlling the recurrence of acute cardiac symptoms following a too rapid diminution of the dosage; and (2) in preparation for tonsillectomy. The side-effects were slight and the damaging influence on the cardiac condition of the disturbance of water and electrolyte metabolism which frequently accompanies cortisone therapy was absent. Within the limits imposed by the small number of cases treated and the short period of observation (80 days), these results suggest that prednisone is a drug of real value in the treatment of rheumatic carditis.

[It is impossible to do justice in an abstract to this well-documented paper, which should be read in the original by those interested.] *V. C. Medvei*

444. **Antimyocardial Antibodies in Rheumatic Fever.** [In English]

V. Rejholec and V. Wagner. *Experientia* [*Experientia (Basel)*] **11**, 278, July 15, 1955. 1 fig., 6 refs.

A brief report on the quantitative estimation of autoantibodies in the serum of patients suffering from rheumatic fever, rheumatoid arthritis, and glomerulonephritis is presented from the Research Institute of Rheumatic Diseases, Prague, and Charles University, Pilsen. Organ antigens were prepared from normal human kidney, myocardium, and liver by extraction

with 1·1% sodium chloride solution and the extracts used to treat collodion particles by Cavelti's method. The "sensibilized" particles were then incubated for one hour at room temperature admixed with geometric dilutions of the patient's serum, and the presence of agglutination determined with an agglutinoscope. Anti-myocardial antibodies were found in the serum at an average titre of 1 in 20 in 6 out of 8 cases of rheumatic fever; at an average titre of 1 in 16 in 8 out of 10 cases of "acute tonsillitis showing the so-called myocardial ECG curve"; and at a titre of 1 in 4 in all of 3 cases of rheumatoid arthritis. These antibodies were present at a low titre in the serum in most of 16 cases of active glomerulonephritis, but in none of 10 cases of latent glomerulonephritis. In a control group of 57 healthy subjects these antibodies were present at a low titre in a small number of cases. It was found that in cases of acute rheumatism the titre of antimyocardial antibodies was reduced as a result of salicylate therapy.

Harry Coke

RHEUMATOID ARTHRITIS

445. Glycine Metabolism in Rheumatoid Arthritis and Allied Diseases

H. M. LEMON, J. M. LOONEY, and W. H. CHASEN. *Rheumatism* [*Rheumatism*] **11**, 48–61, July, 1955. 3 figs., 26 refs.

The high percentage of glycine in the molecules of collagen and elastin compared with those of the other body proteins suggested to the authors that in rheumatoid arthritis and other diseases characterized by lesions affecting the connective tissues glycine metabolism might show some detectable disturbance. Benzoic acid being detoxified by conjugation with glycine and excreted as hippurate by the kidney, they studied the effect on the serum glycine and alanine levels and on urinary hippurate excretion of the intravenous administration of 1·77 g. of sodium benzoate after a 12-hour fast to 91 non-rheumatic control subjects (some had other diseases of bones or joints), 127 patients with rheumatoid arthritis or ankylosing spondylitis, 24 with rheumatic fever or inactive rheumatic heart disease, and 7 with diffuse collagen disease (disseminated lupus erythematosus or scleroderma). Tests of renal and hepatic function were carried out and all patients with gross disorders of these organs were excluded (although 16% of the patients retained had albuminuria and 20% had minor defects of hepatic function as shown by the "bromsulphalein" excretion test or determination of plasma protein partition).

Comparison of the fall in serum glycine levels following the administration of sodium benzoate in the various groups revealed a considerable overlap between the values obtained for the non-rheumatic and rheumatic cases, while even in the same individual marked variations occurred which did not correlate closely with changes in the clinical condition or the erythrocyte sedimentation rate. Statistically significant differences were demonstrated, however, which "can be interpreted best as indicative of reduced reservoirs of readily available glycine in the rheumatoid state, particularly when clinically active disease is present". No such correlation was found between rheumatoid activity and the changes in the serum alanine level or urinary hippurate excretion.

R. E. Tunbridge

446. A Two-year Trial of Combined Treatment with Cortisone and Sodium Pyrocatechol-3-carboxylate in Rheumatoid Arthritis. (Deux années d'essai de l'association cortisone-pyrocatéchol 3 carboxylate de Na, dans la polyarthrite chronique évolutive)

L. MICHOTTE. *Acta physiotherapica et rheumatologica Belgica* [*Acta physiother. rheum. belg.*] **10**, 45–52, March–April, 1955. 3 refs.

The author reports the results obtained in the treatment of 25 patients (8 male and 17 female) suffering from rheumatoid arthritis with cachets each of which contained 6 mg. of cortisone and 320 mg. of sodium pyrocatechol-3-carboxylate; in all but one case not more than 4 cachets were given daily. [The patients' ages are not stated.] Before treatment the patients were classified by the grade of the arthritis and the degree of functional impairment according to the criteria of the International League against Rheumatism, and they were similarly re-assessed at the end of 17 months.

At that time 4 patients had had a remission and had stopped the treatment, in 2 cases medication had to be interrupted as the patients developed cholecystitis and gastric ulcer respectively, while in a further 6 cases the treatment was abandoned in view of the poor response to the low dose of cortisone employed. The results are analysed in a table, which shows that at the beginning of treatment the numbers of patients in Grades I, II, III, and IV were respectively 0, 7, 14, and 4, while at the end of treatment the corresponding figures were 12, 8, 4, and 1.

[A large part of this paper, which might well have been better devoted to giving a more detailed account of the present series of patients, is taken up in comparing the author's results with those recorded in two series reported in the U.S.A. in which no specific treatment was used, and with the report of the American Rheumatic Association on the use of cortisone. The figures quoted from these sources seem to support the author's claim regarding the superiority of the treatment employed in his own small series.]

H. F. Reichenfeld

447. Pneumonia Occurring during ACTH and Cortisone Therapy

J. H. JACOBS and F. C. ROSE. *Tubercle* [*Tubercle*] **36**, 113–118, April, 1955. 5 figs., 9 refs.

In this paper from the Royal Free Hospital, London, 3 cases are reported in which death from pneumonia occurred during ACTH or cortisone therapy for rheumatoid arthritis. In the first case, that of a woman aged 64 years who was admitted to hospital in a semi-comatose condition, there was no history of respiratory symptoms and examination revealed neither bronchial breathing nor adventitious sounds. Hypokalaemia was noted on admission. Death occurred on the fifteenth day despite

treatment with penicillin, potassium chloride, and ACTH. Necropsy revealed generalized oedema of the lungs and lipid infiltration of the zona fasciculata of the adrenal glands. In the second case, that of a woman aged 61 years, there was sudden onset of cough, haemoptysis, and dyspnoea. Crepitations but no bronchial breath sounds were audible, although widespread consolidation was found at necropsy 5 days later. There was an associated monocytic leukaemia. The third patient, a man aged 53 years, had abdominal pain and signs of consolidation at the right base on admission. He underwent laparotomy for suspected perforation because of a previous history of dyspepsia, but no perforation was found; he died 24 hours after the onset of symptoms. Necropsy revealed consolidation at the right base, degeneration of the adrenal glands with haemorrhage into one of them, and 2 small subacute peptic ulcers.

The authors consider that steroid therapy masked the infections, and recommend that when patients receiving ACTH or cortisone develop pneumonia the dosages of the hormones and of antibiotics should be increased.

I. Ansell

448. **Clinical Trial of Metacortandracin [Prednisone].** (Esperienze cliniche con il metacortandracin)
T. GALLI and S. SOLARI. *Minerva medica* [*Minerva med. (Torino)*] **2**, 14–17, July 4, 1955. 6 refs.

At the Medical Clinic of the University of Genoa prednisone (" metacortandracin ") was tried in the treatment of 21 patients, 12 of whom were suffering from rheumatoid arthritis, 1 from gouty polyarthritis in a subacute phase, 1 from early scleroderma, 6 from osteoarthritis with acute pain, and 1 from the " shoulder–hand " syndrome following myocardial infarction, with swelling of the hand and subankylosis of the shoulder. In the 6 cases of osteoarthritis the patients' age and sex are not given; of the remainder, 7 were men and 8 women, their ages ranging between 17 and 75 (but mainly between 30 and 60). Only the short-term results (up to 30 days) are reported and the effect of interruption of the treatment was not studied.

Prednisone was calculated to have an anti-rheumatic effect 4 to 6 times greater than that of cortisone and to be more effective than hydrocortisone. It did not show any influence on water and salt metabolism except for a very slight depression of the serum potassium level. In 2 cases there was an initial increase in the blood pressure, which returned to normal when the dosage was reduced. The dosage (in rheumatoid arthritis) was as follows: 20 mg. daily (in 4 doses) for the first 3 days; 15 mg. for the next 3 days; 10 mg. for 10 days; 7·5 mg. for 4 days; and 5 mg. daily thereafter as a maintenance dose. In no case was epigastric pain, acne, erythema, or psychological disturbance observed. A very slight degree of moon-face developed in 2 cases, and excessive perspiration in one.

The introduction of prednisone is, in the opinion of the authors, a real step forward in the steroid treatment of rheumatic disorders. *V. C. Medvei*

See also Physical Medicine, Abstract 453.

SPONDYLITIS AND SPONDYLOSIS

449. **The C-reactive Protein Test in Ankylosing Spondylitis and in Other Rheumatic Diseases.** (Il " test " della proteina C nella spondilite anchilosante ed in altre malattie reumatiche)
T. LUCHERINI, E. CONESTABILE, P. NATALE. *Reumatismo* [*Reumatismo*] **7**, 214–222, July–Aug., 1955. 3 figs., 14 refs.

In this paper from the Rheumatological Centre of the University of Rome the authors report an investigation into the value of testing for the presence of C-reactive protein in the serum of patients affected by ankylosing spondylitis and other rheumatic diseases. The technique used for the test was that of Hill (*Lancet*, 1952, **2**, 558; *Abstracts of World Medicine*, 1953, **13**, 239), in which the patient's serum reacts *in vitro* with a solution of pneumococcal C-polysaccharide.

Altogether 38 cases were examined, consisting of 19 cases of ankylosing spondylitis, 4 of rheumatic fever, 14 of rheumatoid arthritis, and one of disseminated lupus erythematosus. In rheumatic fever C-reactive protein was constantly present, whereas in rheumatoid arthritis it was present only in the acute phase. In only 5 of the cases of ankylosing spondylitis was a positive reaction obtained, these patients being in the initial phase of the disease, when the activity of the process was indicated by severe clinical manifestations and by a high erythrocyte sedimentation rate. (The reaction was positive in the single case of disseminated lupus erythematosus studied, but this may have been due to superadded pyogenic infection.) Treatment with phenylbutazone had no effect on a positive reaction for C-reactive protein, whereas on substituting treatment with hydrocortisone the reaction rapidly became negative in many cases.

The authors' conclusion is that the test for C-reactive protein is of some value in determining whether the rheumatic process is in an active or a quiescent state.

E. Forrai

450. **The Clinical Manifestations of Spondylochondrosis (Spondylosis) of the Cervical Spine**
J. G. ARNOLD. *Annals of Surgery* [*Ann. Surg.*] **141**, 872–889, June, 1955. 11 figs., 19 refs.

In the view of the author of this paper from the University of Maryland, Baltimore, the term " spondylosis of the cervical spine " is not sufficiently descriptive and the term " spondylochondrosis " is preferable, since it takes into account both the cartilagenous protrusion and the osteophytic overgrowth of the vertebrae. In a review of the literature he points out that rupture of the intervertebral disk has been recognized as a clinical entity since the classic description of Mixter and Barr in 1934. He then describes 10 cases of cervical spondylochondrosis, in 7 of which the long tracts were primarily involved, with resulting paraplegia; in 2 the anterior roots only, producing the " anterior root syndrome "; and in one both the long tracts and anterior roots were markedly involved. The clinical and radiological findings and the treatment are described.

The author then discusses [with excellent diagrams] the anatomy of the spinal canal in the cervical region in 100 cases. The antero-posterior width of the spinal canal of the 5th cervical vetebra was measured, and the average, both in the group as a whole and in those with normal vertebrae, was found to be 1·3 cm., the narrowest being 1 cm. and the widest 1·8 cm. It is suggested that the size of the cervical spinal canal is a significant accessory factor in the causation of symptoms in spondylochondrosis.

Discussing treatment of the condition, the author states that conservative measures are of little or no value unless the lesions are minimal and non-progressive. Minimal symptoms may be present for many years and may then be followed by a fairly sudden exacerbation and marked progression; when this occurs surgical treatment should be given without delay. Laminectomy with section of the dentate ligaments is the treatment of choice; removal of the protruding ridge of bone from the arthritic process is a hazardous procedure. Foramenotomy is indicated where the intervertebral foramen is shown to be tight around the root. The results of operation in the author's series were excellent in 4 cases, moderate in 3, and slight in one. There was no improvement in one case and in one the condition was worse.

[This is a good paper. The author has taken a great deal of trouble, particularly in the anatomical study of the cervical spine.] *Leon Gillis*

COLLAGEN DISEASES

451. Acquired Circulating Anticoagulants in Systemic "Collagen Disease". Auto-immune Thromboplastin Deficiency

P. G. FRICK. *Blood* [*Blood*] **10**, 691–706, July, 1955. 4 figs., 22 refs.

In this paper from the University of Minnesota Hospitals, Minneapolis, the author describes the occurrence of circulating anticoagulants in 3 patients with systemic collagen disease. There was evidence that 2 of the patients were suffering from disseminated lupus erythematosus, while the third was under observation for a drug reaction following antibiotic therapy. Circulating anticoagulants usually give rise to a haemorrhagic state with clinical features similar to haemophilia; in the present cases, however, the clinical manifestation of abnormal haemorrhage was slight in comparison with the laboratory evidence of interference with the coagulation mechanism. In one case there was transplacental passage of the anticoagulant, the latter persisting in the patient's newborn infant for 7 weeks.

The important laboratory features were similar in all 3 cases, and consisted in prolongation of the whole-blood clotting time and recalcification time, and defective prothrombin consumption. It was shown that the addition of a small proportion of the patients' plasma to normal plasma caused a significant lengthening of the recalcification time in the latter. Similarly the addition of the patients' plasma to normal blood caused the prothrombin consumption of the latter to become defective. These findings proved the presence of a circulating anticoagulant. Determination of one-stage clotting time showed that this too was prolonged, and in a mixture consisting of normal and patient's plasma the same phenomenon was observed.

The author concludes that the anticoagulant present in these cases acted as an antithromboplastin, and that its occurrence in association with other manifestations of hypersensitivity and the fact of its transplacental transfer suggest that the mechanism of development was immunological. A subsidiary study showed that circulating anticoagulants were present in 3 out of a series of 30 patients with disseminated lupus erythematosus and allied conditions, an incidence of 10%. The author has little comment to make on treatment, but suggests that prolonged administration of cortisone might have some effect, since "the effect of this drug on other types of immune antibodies like hemagglutinins has been well established".

[In most previously reported cases of circulating anticoagulants the one-stage clotting time has been normal and there has been interference only with blood thromboplastin formation. It is of considerable interest that the interference in the present cases was not only with blood thromboplastin but also with the tissue thromboplastin system, as shown by the prolongation of the one-stage clotting time.] *A. S. Douglas*

452. Roentgenologic Findings in Systemic Lupus Erythematosus. An Analysis of 100 Cases

D. M. GOULD and M. L. DAVES. *Journal of Chronic Diseases* [*J. chron. Dis.*] **2**, 136–145, Aug., 1955. 5 figs., 3 refs.

A large number of cases of systemic lupus erythematosus have recently been studied at the Johns Hopkins Hospital, Baltimore, and from these cases 100 were selected for analysis of the radiological findings. The diagnosis was established by typical clinical findings in 22 cases and histological evidence in the others.

Pleural thickening, usually present at the base of both lungs, was the most frequent abnormality, occurring in 81 cases. Massive effusion was rare. In 52 cases there were lesions in the lung parenchyma, which usually appeared as ill-defined areas of infiltration, although linear plaques were also seen in many cases. Cardiac enlargement, which was present in 53 cases, was due to pericardial effusion in only 3; in the remainder it was thought to result principally from myocarditis. Although joint involvement is a prominent clinical feature of systemic lupus erythematosus the radiographs usually showed only a minimum degree of osteoporosis. Splenic enlargement, which is another clinical feature, was detected radiologically in only 34 patients.

There were a number of other incidental findings, such as impaired renal function on excretion pyelography and lung abscess due to secondary infection. The authors conclude that serial chest radiographs will demonstrate the characteristic features in most cases; they point out that even splenic enlargement was more often detected on well-exposed radiographs of the chest than on radiographs of the abdomen. *D. E. Fletcher*

Physical Medicine

453. Rehabilitation of the Patient with Chronic Rheumatoid Arthritis. A Two-year Study

E. W. LOWMAN. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 628–637, June, 1955. 3 refs.

After briefly reviewing the incidence of and morbidity from the rheumatic diseases in the United States, the author describes an attempt made at the Goldwater Memorial Hospital, New York, to reduce disability by combining rehabilitation with medical treatment during the active phase of the disease process instead of waiting for activity to subside before starting rehabilitation. In a group of 38 patients with chronic rheumatoid arthritis, 18 of whom were severely crippled and 20 less severely disabled, rehabilitation measures were started as soon as the maintenance dosage of cortisone or hydrocortisone had been established, the period of observation in hospital being 7 to 21 months.

Of the 18 severely crippled patients, 7 were totally self-sufficient and 7 partially so when discharged; 4 remained in hospital. All the patients who were less severely disabled were discharged, 15 being totally self-sufficient and 5 partially so. One patient in the former group and 7 in the latter were able to take up full-time employment.

Kathleen M. Lawther

454. The Influence of Electrical Stimulation on the Work Output and Endurance of Denervated Muscle

K. G. WAKIM and F. H. KRUSEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 370–376, June, 1955. 4 figs., 24 refs.

In a study of the output and endurance of denervated muscle carried out at the Mayo Foundation, Rochester, Minnesota, the denervated hind-limbs of albino rats were subjected to electrical impulses of one millisecond duration at a frequency of 16 per second for periods varying from 30 to 480 minutes in 24 hours. A control group was not subjected to stimulation, and another group was left with nerves intact. After 25 to 30 days of this procedure the Achilles tendon of each animal was divided, attached to a 100-g. weight, and stimulated electrically every 3 seconds for several hours, the tendon being connected to a pulley and counter with a timing apparatus which enabled the work output in every 100 seconds to be computed. Finally, the animals were killed and the plantaris, anterior tibial, and gastrocnemius muscles removed, weighed, and their weight compared with that of the contralateral, intact muscles.

It was found that the denervated, unstimulated muscles were capable, on the average, of 7·6% of the work output of the intact muscles, and that they had lost about 75% of their weight at 25 to 30 days after denervation. Electrical stimulation reduced this loss of weight, but not to any great extent; even with stimulation for 480 minutes daily the average weight loss was about 67%. The effect of electrical stimulation was shown by the fact that the work output was 51·8% of normal in muscles stimulated for 480 minutes, 40% of normal in those stimulated for 80 minutes, and 15·7% in those stimulated for 30 minutes per day.

B. E. W. Mace

455. Strength Decrement Index: a New Test of Muscle Fatigue

H. HARRISON CLARKE, C. T. SHAY, and D. K. MATHEWS. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 376–378, June, 1955. 4 refs.

The authors describe, from the School of Physical Education, Springfield, Massachusetts, a new test for determination of fatigue in muscle. In this the strength decrement index (S.D.I.) is determined by relating the decrease in ability to develop tension in a muscle following exercise to the tension developed in the fresh muscle, using the formula:

$$\text{S.D.I.} = \frac{\text{Si} - \text{Sf}}{\text{Si}} \times 100$$

where Si = initial strength before exercise, and Sf = final strength after exercise. The authors have found this a useful test of muscle fatigue, and give examples of its use in tests on men marching and carrying loads under field conditions and in subjects swimming 200 yards against time.

In the marching group the greatest degree of fatigue (highest S.D.I.) was found in the extensor muscles of the trunk, the next greatest being in the elevators of the shoulder; in the latter it was shown that fatigue was significantly greater when the loads were carried low on the back. In the group of swimmers the S.D.I. was determined initially after the subject's first competitive swim, and again after 5 weeks of intensive training. An over-all decrease of about 2% in the S.D.I. was found as a result of this training.

B. E. W. Mace

456. Breathing Exercises in Pulmonary Emphysema and Allied Chronic Respiratory Disease

A. L. BARACH. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **36**, 379–390, June, 1955. 2 figs., 46 refs.

The author describes studies in which it was shown that tilting of the emphysematous patient to an angle of about 20 degrees head down resulted in an increase of elevation of the diaphragm of 3 to 5 cm. and a decrease of pulmonary ventilation of 20 to 25%, as compared with these values in the erect sitting position. This was not accompanied by any fall in arterial blood oxygen saturation or *p*H, or by any increase in its carbon dioxide tension. Relief of dyspnoea was usually immediate. Bending forward to an angle of about 40 degrees also decreased the pulmonary ventilation by about 8%, while the additional application of an elastic belt to the lower abdomen raised this figure to about 20%.

The breathing exercises and ancillary measures employed at the Chest Clinic, Presbyterian Hospital, New

York, are described. Diaphragmatic breathing is taught, and this is augmented by manual compression of the lower thorax, " pursed-lip " breathing, the forward bending posture, and the wearing of a lower abdominal belt. Additional measures to assist the removal of bronchial secretions include the use of bronchodilator aerosols, and deliberate gentle coughing.

B. E. W. Mace

457. **Clinical Aspects of Glossopharyngeal Breathing. Report of Use by One Hundred Postpoliomyelitic Patients**
C. W. DAIL, J. E. AFFELDT, and C. R. COLLIER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 445–449, June 11, 1955. 3 figs., 6 refs.

This report, which comes from the College of Medical Evangelists, Los Angeles, describes the findings in 100 patients with respiratory impairment following poliomyelitis, all of whom had learned the technique of glossopharyngeal breathing. [It is not clear how many patients failed to learn the technique.]

Of 42 patients previously dependent entirely on some type of mechanical respiratory apparatus, all were able to dispense with it for an average of over 3 hours; the vital capacity of these patients showed a mean increase from 7·3% of normal to 39% of normal. A further 27 patients used the technique as an auxiliary aid in breathing and coughing and to avoid fatigue of the usual muscles of respiration; these patients increased their vital capacity from 18% to 49% of normal. The remaining 31 patients employed the method solely for expanding the chest and coughing; they increased their vital capacity from 32% to 60% of normal. The exact time taken to learn the method could not be recorded; some patients learned the trick in one lesson, but most had to spend weeks in practice in order to achieve periods of this type of breathing of any appreciable length, or to be capable of effective coughing and stretching. Some of the patients complained of irritation and drying of the throat, and some of a feeling of faintness when taking a deep glossopharyngeal breath, but otherwise no complications or objections to the method were discovered. Nevertheless the authors did not consider it safe to leave a patient unattended if he depended mainly on this method of breathing, since in the event of pharyngeal spasm glossopharyngeal breathing would become impossible. With this proviso the authors consider that this method of breathing can be of great value in minimizing the effects of respiratory paralysis and in promoting the return of natural breathing.

K. C. Robinson

458. **Changes in Tissue Clearance of Radioactive Sodium from Skin and Muscle during Heating with Short-wave Diathermy. A Preliminary Report**
J. B. MILLARD. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 248–252, July, 1955. 3 figs., 1 ref.

The author reports, from the Devonshire Royal Hospital, Buxton, Derbyshire, the results of the use of radioactive sodium (^{24}Na) for the critical evaluation of the effect of short-wave diathermy on the circulation of the skin and deeper muscular tissues, this effect being determined by observing the rate of disappearance of ^{24}Na from the site of injection. In 46 subjects 5 μc. of ^{24}Na in 0·1 or 0·2 ml. of isotonic saline was injected (1) subcutaneously beneath one of the diathermy electrodes, (2) subcutaneously midway between the electrodes, or (3) in 19 cases to a depth of 2·5 cm. beneath one electrode, into the quadriceps femoris muscle; as a control, similar injections were given in the opposite leg. Skin temperatures at the various sites were recorded at the same time. After a preliminary period of 20 minutes short-wave diathermy was applied for a further 20 minutes with the Bauwens-type electrodes tuned to maximum skin temperature tolerance, and the rates of clearance recorded by means of a scintillation counter. The method employed was essentially that described by Kety (*Amer. Heart J.*, 1949, **38**, 321; *Abstracts of World Medicine*, 1950, **7**, 267).

Examination of the clearance constants showed that the skin clearance rate increased by 150% at the site under the electrode and by 70% in the skin midway between the electrodes; in contrast, the skin clearance rate in the opposite, untreated, leg increased by only 9%. Muscle clearance rates increased under short-wave diathermy by an average of 36%, although considerable variation in the results was noted in the muscle experiments; for example, one patient showed a decrease in the rate of 39%, while 9 had a " cut-off " for periods up to 8 minutes which was, however, followed by a normal or increased clearance rate.

Harry Coke

459. **The Effect of Ultraviolet Irradiation of the Back on the Reflex Regulation of Cardiac Activity.** (О влиянии облучения ультрафиолетовыми лучами на рефлекторную регуляцию сердечной деятельности)
F. Z. MEERSON. *Бюллетень экспериментальной Биологии и Медицины* [*Bjull. eksper. Biol. Med.*] **40**, 33–37, July, 1955. 3 figs., 18 refs.

At the Central Research Institute for Physical Methods of Treatment, Yalta, the following experiments were performed on a total of 30 rabbits. (I*a*) Reflex bradycardia was induced by causing them to inhale ammonia; (I*b*) the same carried out 24 hours after 10 minutes of ultraviolet irradiation from a quartz lamp of an area of 100 sq. cm. on the back, causing the production of an erythematous patch. (II*a*) Tachycardia was induced by the oral administration of 2 minims (0·1 ml.) of 1% solution of nitroglycerin; (II*b*) the same after ultraviolet irradiation as above.

The intensity and duration of the ammonia-induced bradycardia were found to be considerably reduced after irradiation. On the other hand nitroglycerin-induced tachycardia was apparently uninfluenced, or even somewhat exaggerated, by irradiation. Referring to the investigations of Speranski and his collaborators, the author argues that changes in the reflex response of the heart produced by previous irradiation are due not to any chemical substances produced in the erythematous skin, but to the irritation of cutaneous receptors. The electrocardiographic changes following the inhalation of ammonia and ingestion of nitroglycerin are briefly discussed.

A. Swan

Neurology and Neurosurgery

460. **Bell's Palsy. A Clinical and Electromyographic Study**
D. TAVERNER. *Brain* [*Brain*] **78**, 209–228, June, 1955. 13 figs., bibliography.

The literature of Bell's palsy is reviewed and 100 consecutive cases, including examples of the Ramsey Hunt syndrome, studied clinically and electromyographically at the General Hospital at Leeds are discussed. In 45 cases—in 3 of which the paralysis was complete—recovery began 3 to 21 days after the onset and was complete in 18 to 150 days (mean 51 days). There were no sequelae in this group. In the remaining 55 cases recovery was incomplete after periods ranging from 6 months to 3½ years. In 25 of these cases the initial paralysis was complete, and in 49 cases electromyography showed profuse fibrillation, indicating a poor prognosis, 7 to 10 days after the onset. Although voluntary movements began to return after 7 to 180 days (mean 70 days), no patient in this group has recovered completely. There was no significant difference between the two groups in respect of age, sex, and clinical features.

Sequelae in the latter group included contractures (36 cases), " crocodile tears " (6), and associated movements (in all 55 cases). Motor-unit activity in the orbicularis oris muscle occurring synchronously with the eye-blink—" blink bursts "—occurred in all cases and is attributed to misdirection and branching of regenerating axons, as also is the occurrence of associated movements. These findings suggest a more profound lesion than could be caused by simple compression or ischaemia of the facial nerve, while the occurrence of crocodile tears suggests a lesion proximal to the geniculate ganglion—perhaps a parenchymatous neuritis. It is concluded that surgical decompression of the facial nerve is not justifiable in the management of Bell's palsy.

L. G. Kiloh

461. **Variations in the Plasma Fibrinogen during the Course of Multiple Sclerosis**
I. PERSSON. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **74**, 17–30, July, 1955. 16 figs., 25 refs.

At the Nørre Hospital, Copenhagen, the erythrocyte sedimentation rate (E.S.R.) was estimated by the method of Westergren and the plasma fibrinogen content by that of Gram in 9 men and 7 women, aged 22 to 55 years, suffering from disseminated sclerosis, the period of observation varying from 5 to 10 months. The disease had been diagnosed 2 to 24 years before the investigation started.

Compared with the E.S.R., there were variations in the plasma fibrinogen level accompanied by exacerbation of the disease; however, there were periods in which the plasma fibrinogen level was increased without clinical signs of exacerbation. The author points out that although the plasma fibrinogen level is fairly constant in healthy persons, it is raised in most chronic diseases. It is suggested that since the E.S.R. was independent of the plasma fibrinogen level, other factors, such as changes in other serum proteins, may be important in the formation of the thrombi, and that the " periodically raised plasma fibrinogen level as well as the clinical exacerbation is likely to be an accompanying phenomenon to the actual course of the disease ".

G. de M. Rudolf

462. **A New Heredo-familial Neurological Syndrome**
C. C. HARVEY, J. C. HAWORTH, and J. LORBER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 338–344, Aug., 1955. 5 figs., 5 refs.

A new heredo-familial neurological disorder affecting a father and 5 of his children is described with detailed case histories of each. The main features of the condition consisted of athetosis, hypotonia, absent tendon reflexes, extensor plantar responses, mental retardation and periodic febrile attacks occurring in several members of the family with episodes of prolonged unconsciousness.

The possible aetiology of the condition is discussed, and familial recurrent encephalitic illnesses reported in the literature have been reviewed.—[Authors' summary.]

463. **Ischaemic Sensory Loss in Patients with Spinal and Cerebral Lesions**
R. W. GILLIATT. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **18**, 145–154, May, 1955. 4 figs., 5 refs.

In previous work on the effect of artificially produced ischaemia of the arm the author with Wilson (*J. Neurol. Neurosurg. Psychiat.*, 1954, **17**, 104) showed that in the normal subject the mean time required to produce subjective numbness in the fingers was 14 minutes. In the presence of peripheral nerve lesions this " time to numbness " was significantly reduced in the areas of skin supplied by the affected nerve. A similar alteration was noted in patients with dorsal root lesions or peripheral nerve lesions proximal to the site of the restricting cuff. These results suggested that a sensory deficit at any level in the nervous system might be exaggerated by the ischaemic effect of the cuff. In the present paper from the National Hospital, Queen Square, London, the author deals with cases in which there was a known spinal or cerebral lesion. Most of the patients were able to signal the " time to numbness " in the usual way, but in 3 cases in which subjective numbness was already present the end-point was taken as the time at which the patient considered that the sensation aroused by a firm touch was definitely reduced. Changes in the tactile threshold were investigated by means of graded nylon threads.

In all of 5 patients with a cord lesion the " time to numbness " was less than the normal mean figure of

14 minutes, and only in 2 cases did it exceed 10 minutes. One of these cases had been diagnosed initially as cervical spondylosis (although later proved to be one of intramedullary tumour) and during treatment by traction serial ischaemic tests indicated some improvement. In another case serial tests after removal of a neurofibroma at the level of C2 showed a steady increase in the " time to numbness ". In another group of 6 patients with cerebral lesions, 2 of whom had just undergone successful removal of a cerebral tumour, the " time to numbness " was reduced in 3, but in the other 3 there was no such shortening; indeed in one case there was actually an increase in the time, but this was considered to be due to affection of discriminative sensation and a similar lengthening of the time was observed in another patient after the removal of a right parietal tumour.

In discussion the author speculates on the size of lesions necessary to produce detectable sensory loss, the possible effects of two lesions at different levels in the nervous system, the demarcation of doubtful areas of sensory impairment by the production of ischaemia, and the recording of slow sensory changes by serial tests of this nature. It is concluded that the interpretation of the test in the presence of cerebral lesions is attended by certain difficulties, but that in cases of disease of the cord the ischaemia test may provide a sensitive method of assessing improvement or deterioration.

Fergus R. Ferguson

BRAIN AND MENINGES

464. Effects of Anterior Cingulectomy in Man

C. W. M. WHITTY. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 463–469, June, 1955. 5 figs., 10 refs.

Bilateral ablation of the anterior cingulate area (Brodmann's Area 24) in monkeys produces a change in their behaviour towards both man and other monkeys which is manifested mainly by a reduction in aggressive tendencies, loss of fear, and marked reduction in their appreciation of danger. The possibility of applying this operation to man in the form of a subpial ablation by suction of the appropriate area, measuring about $4 \times 1 \times 1$ cm., has been studied at the Radcliffe Infirmary, Oxford. (Detailed anatomical studies are to be published later, but it seems that there are extensive intracortical connexions from this area radiating in all directions.)

As a preliminary step the operation was first tried on 18 chronically deteriorated psychotic patients, mostly schizophrenics, whose behaviour was characterized by obsessional and severe aggressive traits. Sufficient temporary or permanent improvement was obtained in these cases to encourage application of the technique to other patients whose personalities were better preserved, and 7 patients with anxiety or depression and 10 with obsessive symptoms were subjected to the operation. In the former group 2 patients were " greatly improved ", 4 " improved " and able to return to work, and one remained unchanged, while of the 10 obsessive patients 6 were " greatly improved " and 4 " improved ".

The operation is regarded as a major surgical procedure, and its possible advantages must be carefully balanced against the greater simplicity of other techniques, in particular transorbital lobectomy. The danger of producing epilepsy is considered, but is not regarded as serious. Observations made at operation during stimulation and excision of the areas (the patients being conscious) did not lead to any positive conclusions regarding the physiological activity of these areas, nor did comparative observations of the patients in the pre- and post-operative states warrant the attribution of specific or autonomic activity to these areas. The various slight changes observed are described.

L. A. Liversedge

465. Hydatid Cysts of the Brain

R. ARANA-IÑIGUEZ and J. SAN JULIÁN. *Journal of Neurosurgery* [*J. Neurosurg.*] **12**, 323–335, July, 1955. 9 figs., 39 refs.

The authors discuss their experience at the Institute of Neurology, Montevideo, in 13 cases of hydatid disease of the brain. Three of their patients were adults and in them the clinical picture was no different from that of other types of brain tumour. The remaining 10 patients were children under 15, and a similarly high incidence of the disease in early life has been commented upon by other authors. In children the clinical picture is one of intracranial hypertension with somnolence, hemiparesis, and occasional convulsions. The signs of raised intracranial pressure may include craniotabes, and the focal signs are frequently suggestive of an extensive lesion of a cerebral hemisphere, although bilateral tremor and cerebellar signs may lead to the mistaken diagnosis of a posterior-fossa tumour. The diagnosis is suggested by the occurrence of these symptoms in a patient from a rural area in a district in which hydatid disease is known to occur, and in whom intracranial hypertension is associated with signs of a large cerebral lesion, particularly if there is evidence of hydatid disease elsewhere. Accessory methods of investigation such as examination of the blood for eosinophilia and the Casoni and Weinberg reactions were not found helpful in the authors' cases. Electroencephalography reveals an area of absence of electrical activity surrounded by an area of delta activity, and radiographs of the skull show thinning of the cranial vault. Angiography, which is preferable in these cases to ventriculography, reveals an avascular area corresponding to the site of the cyst, with greatly displaced vessels running parallel to the cyst wall suggesting the presence of an enormous spherical mass.

In preference to the separation of the cyst from the cerebrum by gentle dissection or removal of the cyst membrane after instillation of 1% formalin solution, the authors advocate the use of a technique which, they claim, minimizes the risk of leakage of the cyst contents and the consequent production of secondary cysts. After location of the lesion by means of cerebral angiography a broad osteoplastic flap is raised over the site of the cyst. Incisions are made into the brain substance only when necessary, care being taken not to open the cavity in which the cyst is lying. Saline is then injected

gently between cyst and cerebrum until the separation of the cyst is complete and it is expelled. All the authors' patients survived operation. *J. E. A. O'Connell*

466. **The Value of Surgery in Subarachnoid Haemorrhage. A Review of 100 Cases**
G. F. ROWBOTHAM and R. K. HAY. *Newcastle Medical Journal* [*Newc. med. J.*] **24**, 332–337, June, 1955. 2 refs.

A series of 100 consecutive cases of subarachnoid haemorrhage admitted to the General Hospital, Newcastle upon Tyne, was studied by the authors with the primary object of " discovering which cases are suitable for surgical treatment and which type of operation is best ".

Cerebral angiography is considered by the authors to be a prerequisite of surgical treatment, since it is usually impossible by clinical means alone to determine whether the haemorrhage is from a saccular aneurysm or not or to locate its site with precision. The angiogram also provides information about the size of an aneurysmal sac and the shape of its neck. The method which they prefer is the percutaneous injection of the contrast medium into the common carotid artery under local analgesia. Angiography was performed on 88 patients and showed the presence of a saccular aneurysm in 57 and of an angioma in 4, the findings being negative in 27 cases. It was omitted in the remaining 12 cases because of the poor general condition of the patient or the presence of degenerative vascular disease. Negative findings were attributed to the location of the aneurysm in the basilar distribution, to the sac being filled with clot, or to overshadowing of the aneurysm by normal vessels in the routine lateral and antero-posterior views. It is pointed out that there is always some danger that angiography may cause hemiplegia, while in cases of subarachnoid haemorrhage in the acute phase it may intensify the bleeding or reactivate it after its source has been sealed by clotting. Complications, consisting in clouding of consciousness, paralysis of the limbs or eye muscles, dysphasia, or epileptic seizures, occurred in 12 cases. In 9 they cleared within 48 hours, and only in one case could permanent residual hemiplegia be attributed to angiography. The risks which attach to cerebral angiography carried out in the acute phase cannot as yet be fully assessed, but must be taken if surgery is to be contemplated within 24 hours of the onset of haemorrhage.

Of the 57 patients with saccular aneurysm, 34 in whom the immediate prognosis was considered to be better and who were conscious or, at most, only confused were selected for operation. Ligation of the common carotid artery in the neck was performed in 27 cases, intracranial clipping of the anterior cerebral artery in 5, and ligation of the common carotid artery in the neck together with intracranial ligation of the parent artery in 2. One patient died postoperatively and 2 of recurrent haemorrhage. At a follow-up examination 2 months to 3½ years later 29 patients were symptomless or had mild symptoms only, one was " not improved ", and one had had a recurrent haemorrhage. Of the 23 patients with saccular aneurysm who were not operated on, 2 died of the original haemorrhage and 3 of a recurrence, and at the time of follow-up 11 were symptomless or had mild symptoms only, 4 were " not improved ", and 3 had had a recurrence. The authors point out, however, that because of the careful selection of cases for operation the two groups are not comparable. Details of the age and sex distribution and incidence of hypertension in the series are presented in the form of tables.

The authors conclude that in order to minimize mortality from subarachnoid haemorrhage surgical treatment ought to be available in the earliest stages, and that the results of treatment can be substantially improved only by more frequent surgical attack upon the bleeding aneurysm itself. *Marcel Malden*

467. **Effect of Cortisone and Hydrocortisone in Hemiplegia after Cerebral Infarction. 1. Preliminary Report, with Special Reference to Spasticity**
R. F. SHEELY, C. H. JOHNSON, J. J. BAKER, and R. HARBAUGH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 803–806, July 9, 1955. 4 refs.

The incidental observation that cortisone relieved the spasticity in a 62-year-old man who had suffered two cerebrovascular accidents led to the administration of cortisone or hydrocortisone parenterally in 4 further cases of hemiplegia due to cerebral thrombosis at the Annie Warner Hospital, Gettysburg, Pennsylvania. The dosage was 300 mg. on the first day, 200 mg. on the second, 100 mg. on the third, and thereafter 25 to 100 mg. a day for 21 days, 1 g. of potassium chloride three times a day and penicillin being also given. The patients' ages ranged from 59 to 80 and the hemiplegia had been present for varying periods up to 4 months before the treatment began.

The main beneficial effect was seen on the spasticity and pain in the joints of the paralysed side; both these symptoms were diminished, the patients became better able to help themselves, and oedema disappeared from the paralysed limbs. However, contractures and deep reflexes were not affected, nor was there any change in aphasia when this was present. There were no adverse side-effects. In the authors' opinion this treatment is worth further trial. They suggest that one reason for the beneficial effect of cortisone may be the decrease it causes in the permeability of the blood vessels in the damaged area. *G. S. Crockett*

468. **The Results of Surgical Treatment in 27 Cases of Progressive Hydrocephalus in Infancy.** (Résultats obtenus dans le traitement chirurgical de l'hydrocéphalie progressive de l'enfant. A propos de 27 cas)
J. CHAPTAL, C. GROS, R. JEAN, C. CAMPO, and —. VLAHOVITCH. *Pédiatrie* [*Pédiatrie*] **10**, 415–420, 1955.

The authors present the results in 27 cases of hydrocephalus treated by operation at the University Neurosurgical Clinic, Montpellier. In only 5 of these cases was the aetiology definite; in 4 the condition was due to obstetrical or neonatal meningeal haemorrhage and in one to stenosis of the aqueduct of Sylvius. Cases of hydrocephalus secondary to tumour or to meningeal infection were excluded from the series.

Three methods of treatment were employed and are discussed. (1) Removal or cauterization of the plexuses in cases in which hypersecretion was suspected. Among 8 patients thus treated there were 5 deaths, of which 2 were immediate; in 3 patients who survived, the hydrocephalus persisted. (2) Short-circuiting; this is feasible in rare cases which are non-communicating and due, for example, to stenosis of the aqueduct of Sylvius. One such case was treated in this way and cured. (3) In the majority of their cases the authors attempted to establish drainage of the spinal fluid to the peritoneal or pleural cavities, the medullary zone of a vertebra, or through the urinary tract. The efficacy of this procedure is limited by the weak state of these child patients, the great risk of infection, and the uncertainty as to the final anatomical result. In 17 cases ventriculoperitoneal drainage was established by means of nylon catheters inserted subcutaneously down the side of the neck and thorax, a procedure which can be rapidly performed and is not in itself dangerous. Of these 17 patients, 8 died, but not immediately following the operation; of the 9 survivors, good results were obtained in 5 (29% of the total treated), with arrest of the hydrocephalus and normal psychomotor development, some of the patients being observed for over 32 months. The results in the other 4 cases were bad and the hydrocephalus continued to progress.

The possible sequelae of this type of operation are a subcutaneous abscess in the track of the catheter, meningitis, obstruction or displacement of the catheter, and excessive drainage of spinal fluid during the first few days, resulting in marked depression of the fontanelles; this last complication can be prevented to some extent by keeping the child lying down. In 2 cases in which the catheter was dislodged from the peritoneum 12 and 18 months respectively after operation there was no return of intracranial hypertension; the authors suggest it may be possible that some modification of the tissues may occur around the catheter, culminating in the formation of a permanent canal lined by pseudo-epithelium. They admit that this concept has not so far been confirmed histologically; they affirm definitely, however, that certain cases of hydrocephalus do, after several months of development, tend to stabilize themselves spontaneously by the establishment of an equilibrium between the secretion of the choroid plexuses and the capacity for re-absorption. They express their hope that the method of drainage described may tide the patient over the initial phase of expansion without sustaining definitive and often mortal damage to the brain, and so favour the onset of this phase of stabilization. *D. P. McDonald*

469. **Unusual Centrencephalic Seizure Patterns**
D. A. HOWELL. *Brain* [*Brain*] **78**, 199–208, June, 1955. 3 figs., 11 refs.

In this paper from the Montreal Neurological Institute (McGill University) a number of cases of centrencephalic (idiopathic) epilepsy with unusual seizure patterns are discussed, in all of which the electroencephalogram showed classic wave-and-spike activity at 3 c.p.s. either spontaneously or on hyperventilation. In the majority of cases minor seizures without loss of consciousness occurred in which a variety of motor, sensory, or psychical disturbances occurred. Many of the motor phenomena observed were suggestive of a cortical focus; among these were sudden loss of power in an arm, bilateral tremulous movements of the limbs, head-turning, chronic twitching of a limb or of one side of the face, staring, blurring of vision, inability to swallow, and chewing movements—all without impairment of consciousness or amnesia. Sensory phenomena were less common, but vertigo, a high-pitched whistling noise, and blindness were experienced, while epigastric sensations, feelings of choking, constriction of the chest, and of progressive slowing of the heart, and a warm, prickling sensation in the head also occurred. Among the psychical phenomena reported were a sense of impending death, a " funny faraway feeling ", hallucinatory experiences, and inability to speak. Two patients had attacks in which they could hear conversation but could not understand it. In a second group of cases a transient hemiparesis followed a major convulsion.

The author emphasizes the surprising frequency with which centrencephalic seizures mimic those due to focal cortical discharges, though he admits that in some cases an additional cortical focus may be present which has not been disclosed by electroencephalography. It would appear that the spread of a discharge of central origin may be restricted and asymmetrical; if this resulted in the discharge reaching a small area of cortex only, the resulting attack would mimic a focal cortical discharge. *L. G. Kiloh*

470. **The Hippocampal Formation in Temporal Lobe Epilepsy**
A. MEYER and E. BECK. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **48**, 457–462, June, 1955. 6 figs., 30 refs.

After a brief summary of published work on the functional significance of the hippocampal formation, an area which has recently assumed unexpected practical importance as a result of the operation of anterior temporal lobectomy, the authors recall the work of Penfield and his associates which led these workers to postulate that incisural sclerosis was the prime cause of all epilepsy not attributable to actual focal lesions, and to the conclusion that this sclerosis was due to herniation at birth. This coincidence of sclerosis of Ammon's horn with clinical or encephalographic indications of temporal lobe epilepsy was also established by Sano and Malamud.

The authors then present an account of 20 of their own cases seen at the Maudsley Hospital, London, which showed features comparable to the incisural sclerosis of Penfield. In 18 of these a biopsy specimen of tissue from Ammon's horn was examined, but only in 12 cases was sclerosis of a degree comparable to the findings of Sano and Malamud observed. Examination was also made of the amygdaloid nucleus, and in 4 of the few cases in which appropriate material was available focal or diffuse loss of neurones with subsequent gliosis was noted.

Two further cases are also described in which severe status epilepticus had been a feature during life and in both of which the cornu ammonis and the amygdaloid nucleus showed selective sclerosis at necropsy. It seems possible that the amygdaloid nucleus and adjacent tissues may play an important part in the production of temporal lobe seizures, at least in the severest type of cases, but the authors prefer to postpone detailed discussion of the probable pathogenetic events to a later stage of the investigation. *L. A. Liversedge*

NEUROMUSCULAR DISEASES

471. **Procaine Amide in the Treatment of Myotonia**
N. GESCHWIND and J. A. SIMPSON. *Brain* [*Brain*] **78**, 81–91, 1955. 3 figs., 16 refs.

It is argued that since electromyography shows the delayed relaxation of myotonia to be associated with fast, repetitive action potentials in the affected muscle fibres, any drug preventing neuromuscular transmission can control the myotonia only by reducing voluntary innervation of the muscle, and that a drug is needed which will "stabilize the polarized membrane of the muscle fibre so that repetitive firing will not occur following normal innervation". On this basis, 2 patients with dystrophia myotonica were treated at the National Hospital, Queen Square, London, with procainamide in doses of 800 and 1,000 mg. respectively at a rate of 100 mg. a minute. This abolished active myotonia, reduced "needle" myotonia, and did not appreciably alter percussion myotonia. Oral administration was then tried, and was successful in 9 cases in abolishing or greatly reducing active myotonia, the dose required being about 1 g. 4 times a day. Relapse occurred within 24 hours if the drug was withdrawn. Side-effects, in particular nausea, occurred in 5 patients, but were not sufficiently severe to necessitate stopping the treatment.
J. W. Aldren Turner

472. **Periodic Paralysis.** (La paralysie périodique)
M. BECCUAU, J. VELLUZ, J. DELGA, and R. COIRAULT. *Annales de médecine* [*Ann. Méd.*] **56**, 437–450, 1955. 3 figs., 25 refs.

Periodic paralysis is a rare but not new disorder, the first description of it being attributed to the London physician Musgrave in 1727. In this paper from the Military Hospital of Val-de-Grâce, Paris, the authors describe 3 cases in young soldiers aged 20 to 23 and discuss the mechanism of the disease. One of the cases was of the familial type, in which the disease could be traced back as far as the patient's great-grandparents, but the other 2 were sporadic cases with no specific family history. The detailed clinical accounts of all 3 cases illustrate the sudden attacks of paralysis, amounting on some occasions to a complete quadriplegia. Generally the facial muscles were spared, and no sensory loss and no psychological changes were observed. Characteristic electromyographic findings during and after an attack are recorded and illustrated. Laboratory investigations showed that the blood potassium content was invariably reduced during an attack, returning to normal as the paralysis disappeared and remaining within normal limits between attacks. The urinary excretion of potassium was within normal limits; in one case the rate of urinary excretion of creatinine was observed to fall during an attack, but this was followed by a compensatory rise the next day.

In the treatment of these cases potassium was first tried, but was later replaced by adenosine triphosphate (A.T.P.) with good results. Within 15 minutes of injecting 20 mg. of A.T.P. intravenously objective improvement was noted, the attack began to abate, and symptoms cleared within 2 hours, whereas previously the usual duration of an attack had been 6 to 8 hours. After a week of intravenous administration the drug was given orally in doses of 3 mg. three or four times daily. The authors consider that the immediate cause of the paralysis is a deficiency of A.T.P. in the muscle cells. This in turn derives from a disturbance of potassium metabolism, of which the commonest expression is the presence of hypokalaemia. They note, however, that there have been reliable reports in the literature of normal or even raised blood potassium levels in this condition. This they explain by assuming that in such cases the potassium is stored in the cells in an inactive form, and thus a functional potassium deficiency could still occasion a defect in the synthesis of A.T.P., which is an essential metabolite in the contraction of muscles.
William Hughes

473. **Treatment of Muscular Atrophies with Amino Acid Mixtures**
K. OJI, K. ILEGAWA, S. IMOTO, and T. YOSHIDA. *Medical Journal of Osaka University* [*Med. J. Osaka Univ.*] **6**, 291–308, March, 1955. 9 figs., 22 refs.

The authors have treated 13 cases of muscular dystrophy, 4 of progressive muscular atrophy, and 6 of amyotrophic lateral sclerosis for periods of 3 to 12 weeks with daily intravenous infusions of a mixture of amino-acids consisting of 100 to 200 ml. of 5% casein hydrolysate, 20 to 40 ml. of 2% DL-methionine, 20 to 40 ml. of 10% glycine, and 40 ml. of 20% glucose. It is claimed that in the cases of muscular dystrophy strength improved and atrophic muscles increased in volume and limbs in circumference; improvement was most striking in adults and in early cases, less so in children and in late cases. Patients with progressive muscular atrophy also improved, though to a less striking degree; the least improvement was obtained in the patients with amyotrophic lateral sclerosis. An improvement in creatine tolerance occurred in all cases when glycine was omitted from the mixture.

[No attempt was made to control this therapeutic trial, and the results are unconvincing. In the hands of other workers similar treatment has proved to be of no value. The authors also describe abnormalities of chronaxie and of glucose tolerance in their patients with muscular dystrophy, and claim that these too were improved following treatment; however, many previous workers have failed to find such abnormalities in this disease.]
John N. Walton

Psychiatry

474. **The Content of Phosphopyridine Nucleotides in the Blood of Patients Suffering from Neuroses and Organic Diseases of the Nervous System.** (О содержании фосфопиридинуклеотидов в крови больных неврозами и органическими заболеваниями нервной системы)
S. A. DMITRIEVA, L. B. GAKKEL, and A. M. PETRUNKINA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 501–504, 1955. 2 figs., 5 refs.

As the clinical picture of pellagra in its early stages resembles that of neurasthenia it was decided that estimation of the content of nicotinic acid derivatives in the blood of neurotic patients might prove of interest. The levels of codehydrogenases I and II (active derivatives of nicotinic acid) were therefore measured in the blood of 162 patients suffering from various neuroses, in 29 patients with organic nervous disease, and in 10 healthy subjects. It was found that the blood codehydrogenase levels in most of the neurotic patients were near the lower limit of normal or below it. When the results were analysed according to the nature of the clinical picture the blood codehydrogenase levels appeared to be lowest in patients with predominantly depressive symptoms. *L. Crome*

475. **Variability of Mongolism**
A. LEVINSON, A. FRIEDMAN, and F. STAMPS. *Pediatrics* [*Pediatrics*] **16**, 43–54, July, 1955. 15 figs., 12 refs.

Having observed many individual differences in the physical features and developmental behaviour of children with mongolism, the authors, at the Cook County Hospital, Chicago, undertook a systematic investigation of the frequency of the variations in 50 mongol children.

The majority of the patients (27 males and 23 females) were under 11 years of age when the investigation began. Ten were prematurely born, weighing under 2·5 kg. at birth; the authors state that in the group as a whole there was greater variation in birth weight than in normal infants. In 32 of the 50 the condition was diagnosed before the age of 6 months. A study of the developmental history revealed that 25 out of 35 held the head up by the age of 10 months, 29 out of 46 sat up by 12 months, and 26 out of 40 walked by the age of 2 years. The first tooth had erupted by one year in 26 out of 35, and the first words been spoken by 26 out of 40 by the age of 2½ years. In 32 of the 50 cases the mother was over the age of 30 when the mongol child was born, and in 38 the mongol was a 1st, 2nd, or 3rd child. The most frequent characteristics were a flat occiput (41), red cheeks (33), rough cheeks (37), slanting eyes (44), small or absent lobe of the ear (40), flat nasal bridge (31), constantly open mouth (31), fissured lips (28), small teeth (28), irregular alignment of teeth (34), high-arched palate (37), flat nipples (28), diastasis recti (38), hyperextensible joints (44), hypotonic muscles (33), short and broad hands (37), flabby hands (42), short fingers (35), tapering fingers (26), short little finger (33), and curved little finger (34). Constipation, frequent colds, and blepharitis were common complaints. In 30 (out of 44) the electroencephalogram was normal or borderline. *G. de M. Rudolf*

476. **Radioiodine Uptake in Children with Mongolism**
A. FRIEDMAN. *Pediatrics* [*Pediatrics*] **16**, 55–66, July, 1955. 5 figs., bibliography.

The radioactive iodine (^{131}I) uptake of the thyroid gland was studied at Cook County Hospital, Chicago, in 61 unselected children with mongolism and 68 mentally retarded euthyroid children. Care was taken to exclude any child in whom thyroid function might be disturbed. The ages of the mongols (35 males and 26 females) ranged from 6 months to 16 years and of the controls (36 males and 32 females) from 2 to 16 years. Thyroid medication, which had previously been given to the mongols for long periods of time, was withdrawn 10 to 14 days before the investigation started.

A dose of 10 to 20 microcuries of ^{131}I with a half-life of 8 days was given by mouth to the non-fasting child, the proportion taken up by the thyroid gland being measured 24 hours later. Measurements were made, at a constant distance of 20 cm. between the distal end of the Geiger–Müller tube and the skin, over the thyroid isthmus and over the thigh (immediately above the knee). The total radioactivity administered was estimated by subtracting the "background" count from the tracer-dose count. The radioactivity of the thyroid gland was determined by subtracting the thigh count from the neck count, 9% being added to the neck count to compensate for decay in activity during the 24 hours.

A near-normal distribution of cases according to the ^{131}I uptake, extending over the 6% to 40% range with a peak at 21% to 25%, was obtained in both mongols and controls. There was an uptake of 25% or less in 44 of the mongols and in 54 of the controls, but statistical analysis showed that no real difference existed between the two groups. About two-thirds of the patients in each group fell in the euthyroid range; of the remaining one-third, more patients were in the low borderline than in the high borderline group, but none was definitely hypo- or hyperthyroid. No significant correlation was found in either group between ^{131}I uptake and age and sex of the patient, nor in the mongols between ^{131}I uptake and the I.Q.

No temporary suppression of thyroid function was observed in the mongols following cessation of thyroid medication; the author suggests that this may have been due to the small dose administered (½ grain (32 mg.) twice or three times a day). [He does not discuss whether suppression of a high uptake could have occurred.] *G. de M. Rudolf*

477. **Clinical Studies on α-(2-Piperidyl) Benzhydrol Hydrochloride, a New Antidepressant Drug**
H. D. FABING, J. R. HAWKINS, and J. A. L. MOULTON. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 832–836, May, 1955. 1 fig., 2 refs.

A clinical trial of a new antidepressant drug, α-(2-piperidyl) benzhydrol hydrochloride ("meratran"), in 320 ambulatory patients suffering from various neuropsychiatric conditions is reported. The drug was superior to drugs of the amphetamine series because it seldom interfered with sleep, appetite, or cardiovascular responses. In a dosage of 1 to 25 mg. daily it was of value in the majority of patients with reactive depression and in more than half of those with mild endogenous depression; agitated depressive states did not respond favourably. No therapeutic effect was noted in anxiety states and schizophrenia. *F. K. Taylor*

478. **The Effect of "Meratran" on Twenty-five Institutionalized Mental Patients**
J. W. SCHUT and H. E. HIMWICH. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **111**, 837–840, May, 1955. 3 refs.

"Meratran" [see Abstract 477] was given to 25 patients in hospital suffering from chronic psychiatric disorders; most of the patients were over 50, and 19 had schizophrenia. A variable degree of improvement was observed in retarded and depressive states in response to a dosage of 2·5 mg. once or twice a day. The drug appeared to be contraindicated in patients with delusions, anxiety, and cerebral arteriosclerosis. *F. K. Taylor*

479. **Chlorpromazine, Reserpine, and Isoniazid Treatment in Mental Disorder. A Preliminary Communication**
J. K. HEWAT, P. W. W. LEACH, and R. W. SIMPSON. *British Medical Journal* [*Brit. med. J.*] **2**, 1119–1120, Nov. 5, 1955. 12 refs.

480. **Effects of Modified E.C.T. on the Electrocardiogram**
R. GREEN and A. WOODS. *British Medical Journal* [*Brit. med. J.*] **1**, 1503–1505, June 25, 1955. 14 refs.

An electrocardiogram (ECG) was recorded before, during, and after electric convulsive therapy (E.C.T.), given to 105 patients on 214 occasions at St. George's Hospital, London. Thiopentone and large doses of suxamethonium chloride (1·6 mg. per kg. body weight) were used to give complete relaxation and ensure clear records. Ten of the patients had clinical or ECG evidence of some cardiac abnormality, including old infarction, mitral stenosis, right bundle-branch block, left ventricular hypertrophy, and complete heart block; no serious incidents occurred in these cases. The effects of the shock on the ECG are discussed in detail and the relevant literature carefully reviewed.

From the present investigation the major conclusions (which confirm previous findings and clinical experience) are that the strain of E.C.T. on the heart is less than was originally anticipated; that sinus tachycardia is usual, and may be useful in differentiating between stunning and shock; that premature beats, usually ventricular, occur more frequently (in 39% of cases) than has previously been reported, most of them during the convulsive phase; and therefore that where the presence of heart disease suggests that gross arrhythmia is likely to occur quinidine or procainamide may be of prophylactic or therapeutic value [though the use of these drugs in any of the authors' cases is not reported]. *A. C. Tait*

481. **Clinical Observations on the Use of Electrically Induced Sleep in the Treatment of Mental Patients.** (Клинические наблюдения по лечению электросном психически больных)
M. V. KORKINA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 520–523, 1955. 3 refs.

The author reports experience gained in the use of electrically induced sleep in the treatment of 63 cases of psychosis at the Second Moscow Medical School. The electrodes were placed over the occiput and the orbit and an intermittent current of 5 to 10 mA was applied at a rate of 1 to 20 impulses per second, each impulse lasting 0·2 to 0·3 millisecond. Treatment was given daily (except on Sundays) for 10 to 25 days, the duration of the periods of sleep increasing from 10 to 15 minutes to 2 to 2½ hours, to 36 patients with schizophrenia, 26 with psychoneurosis, 9 with cyclical psychoses, 6 with presenile psychoses, and 6 with organic disease of the central nervous system. The treatment proved valuable, particularly in the so-called marginal states—that is, in psychogenic reactions and some forms of neurosis. It was more effective in the hallucinatory and hallucinatory-paranoid forms of schizophrenia than in its hypochondriacal and purely paranoid forms. The results in the cyclical psychoses were fairly good, particularly when sleep was combined with other forms of treatment. It was unsuccessful in the presenile psychoses, various hypochondriacal states, and in simple schizophrenia. Its effect in obsessional states was only temporary. This treatment is completely harmless and hardly ever contraindicated by visceral disease. *L. Crome*

482. **Prolonged Sleep Treatment in Obsessional States.** (К вопросу о лечении удлиненным сном навязчивых состояний)
S. N. DAVIDENKOV, S. N. DOTSENKO, and M. K. YAKOVLEVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **55**, 505–510, 1955. 10 refs.

Contradictory results have been reported from the use of prolonged sleep in the treatment of obsessional states. The authors apply prolonged sleep for either 5 or 10 days initially, repeating it after a short interval for a further 5 days. They induce sleep by means of drugs in combination with conditioned reflexes and sometimes hypnosis, the patients being treated in special wards. Psychotherapy is also given in all cases. Of 17 patients with obsessive signs (13 women and 4 men), 13 had phobia, 3 compulsive movements, and one obsessive ideas; 15 were classified as neurasthenic and 2 as hysteric. Treatment was successful in 14 cases and failed in 3. *L. Crome*

Dermatology

483. **Prednisone in Treatment of Selected Dermatoses. Preliminary Report**
H. M. ROBINSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **158**, 473–475, June 11, 1955. 1 ref.

The value of the synthetic steroid prednisone (" meticorten ") in the therapeutic management of pemphigus vulgaris, systemic lupus erythematosis, exfoliative dermatitis, and atopic dermatitis is discussed. Before the beginning of treatment the diagnosis was confirmed by biopsy. The method of administration of the drug and the satisfactory results obtained in 5 patients who had previously received steroid therapy and in 6 who had not are described in detail. No serious side-effects were noted, and there was no significant change in the blood picture, the electrolyte balance, or the blood sugar level.
G. B. Mitchell-Heggs

484. **Alseroxylon in the Treatment of Pruritic and Psychogenic Dermatoses**
R. J. FERRARA and H. PINKUS. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **72**, 23–28, July, 1955. 19 refs.

" Alseroxylon " is a concentrate of the active alkaloids in the root of *Rauwolfia serpentina*. At Detroit Receiving Hospital, Detroit, Michigan, 36 patients with dermatoses in which a definite psychogenic factor was apparent were given alseroxylon for periods of 2 to 6 weeks, or in courses alternating with a placebo for up to 14 weeks; the daily dose was 4 to 8 mg. All the patients became relaxed, tranquil, and mildly sedated, and 7 out of 10 with insomnia were greatly benefited. The most notable effect was the relief of pruritus, only one patient with urticaria experiencing no relief in this respect. In patients with neurotic excoriations and trichotillomania the results were consistently excellent. Other patients, in whom the psychogenic factor did not appear to be causal, showed relief from itching and a 50 to 100% improvement in the skin condition. Subjective improvement generally began in 3 to 7 days and the maximum therapeutic response occurred in from 1 to 4 weeks. It was noted that symptoms tended to return in a number of cases after 1 to 4 weeks of placebo therapy. Side-effects, apart from severe fatigue in one case, were slight, and included drowsiness, nasal congestion, increased appetite, slight diarrhoea, disturbing dreams, thirst, and nocturia.
E. H. Johnson

485. **Aminopterin for Psoriasis**
R. B. REES, J. H. BENNETT, and W. L. BOSTICK. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **72**, 133–143, Aug., 1955. 5 figs., 9 refs.

Although aminopterin (4-amino-pterylglutamic acid) is a potentially dangerous drug, it has a favourable effect on the lesions in psoriasis. Toxic reactions may be neutralized by intramuscular injection of 3 mg. of citrovorum factor daily for 2 or 3 days. By interfering with the metabolism of folic acid, aminopterin retards the proliferation of epithelial cells; this is beneficial in psoriasis, in which epithelial proliferation and keratinization are accelerated. Patients with psoriasis were given various dosages of aminopterin in an attempt to determine the most effective and the least toxic dosage. When 0·5 mg. was given daily by mouth, to a total of not more than 6 mg. in 12 to 20 days, there was great improvement in the lesions in 80% of cases, mild toxic effects—sore mouth, temporary alopecia, skin erosions, leucopenia, and mild diarrhoea—being observed in 8%. Topical application of an ointment containing 1% of aminopterin was ineffective.
E. Lipman Cohen

486. **Evaluation of Antibiotics in the Control of Pustular Acne Vulgaris**
F. T. BECKER and M. G. FREDRICKS. *Archives of Dermatology* [*Arch. Derm.* (*Chicago*)] **72**, 157–163, Aug., 1955. 8 refs.

Oral administration of certain antibiotics was tried at Duluth Clinic, Duluth, Minnesota, in the treatment of 154 patients suffering from pustular, cystic, or nodular acne. The best results were achieved with tetracycline in a dosage of 250 mg. 4 times a day for 2 days, then twice daily for about a week, only 1 out of 37 patients experiencing nausea and diarrhoea severe enough to warrant cessation of treatment. Erythromycin was the next most effective antibiotic, favourable results often being obtained with 200 mg. every 6 hours, provided treatment was continued for 2 or 3 weeks. Carbomycin was well tolerated, but large doses (1 to 2 g. daily) had to be given for at least a month in order to obtain good results. The authors conclude that oral administration of these antibiotics is a useful adjuvant to other methods of treating acne, including dietary restriction, topical applications, and *x*-ray therapy. Other helpful measures are weekly injections of staphylococcal toxoid and the addition of neomycin to the usual acne lotions in a strength of 5 mg. per ml.
E. Lipman Cohen

487. **Pseudopelade of Brocq: its Relationship to Some Forms of Cicatricial Alopecias and to Lichen Planus**
J. GAY PRIETO. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **24**, 323–335, March, 1955. 16 refs.

In this paper from the University of Madrid an attempt is made to clarify the confusion which exists concerning the relationship between pseudopelade of Brocq and lichen planus and some forms of cicatricial alopecia, the author describing his own concept and also the delimitations of these conditions and of the Graham-Little syndrome. He concludes that a number of diseases of the scalp may produce in the final stages some forms of cicatricial alopecia clinically identical with pseudopelade, and that these processes should be regarded as " pseudopelade states " as suggested by Degos.
G. B. Mitchell-Heggs

Paediatrics

488. Physique and the Grammar School Entrance Examination

R. W. PARNELL, G. E. PEIERLS, C. C. STANDLEY, and C. K. WESTROPP. *British Medical Journal* [*Brit. med. J.*] 1, 1506–1510, June 25, 1955. 8 figs., 6 refs.

During the period January, 1953, to March, 1954, 371 boys and 421 girls aged 11 years from the City of Oxford schools were examined and classified by Sheldon and Tucker's somatotype method. Since the technique used was based upon physical measurements instead of photoscopic methods and in the absence of photographic standards, the three components were named "fat" (endomorphy), "muscularity" (mesomorphy), and "linearity" (ectomorphy). The marks subsequently obtained by these children in the grammar school entrance ("11-plus") examination were then studied in relation to the distribution of physical types. The examination consisted in 1953 of an intelligence test and papers in English and arithmetic, to which the Peel test of practical ability was added in 1954, being taken by approximately two-thirds of the children studied. The omission of 35 boys and 21 girls who either failed in the intelligence test (and were therefore excluded from the rest of the examination) or were absent from one or more papers (absence being significantly more frequent than the average among girls with a high fat rating and less frequent among boys of linear build) reduced the total numbers studied to 336 boys and 400 girls.

It was found that among the girls the less muscular sectors of somatotype distribution, especially the linear-fat sector, contained significantly higher proportions with marks above the average, this being consistent for all four tests. A similar, though less marked, trend was found among the boys, those in the fat and linear-non-muscular sectors doing significantly better than the remainder in English and arithmetic. In spite of this tendency of the examination to select less muscular children, a higher proportion of those who won places—both boys and girls—were considered by their teachers to be good at games than of those who did not.

The authors point out that a superior examination ability among linear subjects with more than average fat for their weight was also found among Oxford undergraduates taking the final honours examinations (Parnell, *Brit. med. J.*, 1954, **2**, 491). Since there is a significant relationship between this type of physique and a comparatively high disposition to psychological breakdown, a high prevalence of such upsets would be expected as an associated consequence of intensive academic selection. *R. J. Matthews*

489. An Anthropometric Study of Edinburgh Schoolchildren

H. S. PROVIS and R. W. B. ELLIS. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **30**, 328–337, Aug., 1955. 6 figs., 17 refs.

NEONATAL DISORDERS AND PREMATURITY

490. Further Studies on the Effects of Hypoxia on the Respiration of Newborn Infants

H. C. MILLER and N. W. SMULL. *Pediatrics* [*Pediatrics*] **16**, 93–103, July, 1955. 2 figs., 13 refs.

It has been shown by the authors (*Pediatrics*, 1954, **14**, 93; *Abstracts of World Medicine*, 1955, **17**, 153) that whereas infants several weeks old respond to hypoxia with an increase in minute and tidal volumes and in respiratory rate, when newborn infants are kept in an atmosphere of diminished oxygen tension (10 to 12%) a steady decline in respiratory volumes and rate takes place, suggesting that the chemoreceptor reflexes are relatively inactive in the newborn infant. Cross and his co-workers, however, reported an initial hyperventilation followed by a fall in respiratory volume and rate, and take the view that the chemoreceptor reflexes are active at birth, but that the medulla becomes unresponsive after about 2 minutes so that the infant is unable to sustain the hyperventilation.

This difference of opinion may have been due to failure on the part of the latter workers to take the age of the infant into account. Using a face mask instead of a body plethysmograph for the measurement of respiratory volumes, the present authors have therefore studied the effects of exposure to diminished oxygen tension on 8 newborn premature infants and compared them with the effects on 9 newborn full-term infants. Subsequently the tests were repeated with 9 older premature babies (12 to 84 days). In both premature and full-term infants in the first 2 days of life hypoxia failed to produce any hyperventilation, while in the older infants hyperventilation occurred, but was poorly sustained. The explanation put forward is that the chemoreceptor reflexes at birth are insufficiently strong to stimulate the medullary centres and only increase in strength gradually over a period of months.

Wilfrid Gaisford

491. Premature Induction of Labour in the Treatment of Haemolytic Disease of the Newborn

G. A. KELSALL and G. H. VOS. *Lancet* [*Lancet*] **2**, 161–164, July 23, 1955. 14 refs.

The authors record their experience at the King Edward Memorial Hospital for Women, Subiaco, Western Australia, over a 4-year period in the treatment of haemolytic disease of the newborn by exchange transfusion and the premature induction of labour, when indicated, in 246 pregnancies in which the mother's serum contained abnormal Rh antibodies against the infant's erythrocytes. Of the 246 babies, 23 were delivered, either spontaneously or by induction of labour, before the 35th week of gestation, and 112 by induced labour between the 35th and 40th weeks.

The over-all mortality for the spontaneous deliveries was 34·6% (45 out of 130) and for the induced labours 12·9% (15 out of 116), or excluding the infants delivered before the 35th week, 23·4 and 10·7% respectively. These figures are compared with the results obtained by Mollison and Walker (*Lancet*, 1952, **1**, 429) who reported mortality rates of 24·1% for spontaneous and 36·4% for induced deliveries, the latter figure showing a striking difference from the mortality (10·7%) among similar cases in the present series (although it is carefully pointed out that for a number of reasons the two series are not strictly comparable). The authors state that in their experience kernicterus has become so rare among infants born of prematurely induced labour " as to be practically never seen ", and that their treatment has virtually eliminated stillbirths after 35 weeks' gestation. They stress the importance of avoiding citrated stored blood for exchange transfusions since this may cause tetany and cardiac inhibition owing to the lack of calcium and the often dangerously high content of potassium in stored blood; they use instead freshly collected, warm, heparinized blood. The time of induction of labour is related, in the absence of other indications, to the results of the antiglobulin titration [but the details of this relationship are not given].

The follow-up of these patients is not complete and a further report is promised later. *R. M. Todd*

492. **Observations on the Convalescent Phase of Erythroblastosis Fetalis**

C. B. HYMAN and P. STURGEON. *Pediatrics* [*Pediatrics*] **16**, 15–23, July, 1955. 3 figs., 19 refs.

At Los Angeles Children's Hospital (University of Southern California) 20 infants suffering from haemolytic disease of the newborn, half of whom had received an exchange transfusion of Rh-positive and half of Rh-negative blood, were studied during a subsequent period of 4 to 6 months.

During the first 2 months there was a decrease both in blood haemoglobin concentration and in total body haemoglobin content (calculated on the assumption that the body contained 40 ml. of blood per pound (88 ml. per kg.) body weight). Later, however, the total haemoglobin content began to increase although the blood haemoglobin level continued to fall or remained stationary. Reticulocytosis in the infants given Rh-positive blood became evident during the fourth week of life, reaching a peak about the eighth week. In those given Rh-negative blood it was delayed until the fifth week. When Rh-positive blood was used for the exchange transfusion the reaction to the Coombs test became weaker but remained positive for 5 to 6 weeks. With the Rh-negative blood the reaction became negative within 3 days. Return to the Rh-positive state was delayed after exchange with Rh-negative blood for 19 to 39 days.

The important point is brought out by this study that later transfusions (during the anaemic period) are not necessary if the total body haemoglobin content is rising, unless the haemoglobin level in the blood is too low for the safety of the infant (that is, less than 6 to 8 g. per 100 ml.). The authors found no evidence of erythroid hypoplasia in their cases except in the very early stages, when it was evidenced by the delay in the appearance of reticulocytosis and in the return to the Rh-positive state. *Wilfrid Gaisford*

493. **Melena Neonatorum. An Experimental Study of the Effect of the Oral Administration of Blood on the Stools**

L. APT. *Journal of Pediatrics* [*J. Pediat.*] **47**, 1–5, July, 1955. 1 ref.

The cause of bloody stools in the newborn is not always clear. The author has therefore investigated the effect of the intragastric administration of blood on the stools of newborn babies at the Children's Medical Center, Boston. Blood was given by stomach tube at the rate of 1 ml. per minute in amounts varying from 10 to 40 ml. to babies a few hours old, and also to other infants about 4 days old after the passage of meconium had been completed. With the guaiac test blood could be detected in the stools as early as 7 hours after its introduction, and the test did not become negative in some cases until 80 hours later. Grossly bloody stools were passed by the newborn infants about 9 hours after the introduction of 35 ml. of blood, but a much smaller volume (about 10 ml.) was required to produce a similar result in the 4-day-old babies. The stools of a control series of 35 infants of similar age not given blood were also examined daily during the first 5 days of life, but no occult blood was detected.

R. M. Todd

494. **" Melena " Neonatorum: the Swallowed Blood Syndrome. A Simple Test for the Differentiation of Adult and Fetal Hemoglobin in Bloody Stools**

L. APT and W. S. DOWNEY. *Journal of Pediatrics* [*J. Pediat.*] **47**, 6–12, July, 1955. 8 refs.

Grossly bloody stools in the newborn infant may result from swallowed maternal blood or from bleeding into the infant's gastro-intestinal tract. A test to differentiate blood coming from these two sources, which depends upon the different reactions of adult and foetal haemoglobins to alkali, has been developed at the Children's Medical Center, Boston, and is here described. A solution of the stool in 5 to 10 parts of water is mixed with 1% sodium hydroxide and the change in colour is observed after centrifugation for 2 minutes. If adult haemoglobin is present the colour changes from pink to a brownish-yellow, but if the blood is foetal the colour remains predominantly pink. A control test should be performed simultaneously, using the infant's own peripheral blood. The test is not reliable with " tarry " stools, in which the oxyhaemoglobin has already been converted to haematin.

In order to establish the validity of the test 6 infants were given sufficient blood by stomach tube to produce grossly bloody stools, cord blood being given to 3 of them and adult blood to the other 3. The two types of haemoglobin in the stools were identified correctly by the alkali method. A further 13 infants were also investigated, 7 of whom were thought to have swallowed

maternal blood—a conclusion reached on clinical and haematological grounds; the haemoglobin–alkali test gave a positive reaction for adult haemoglobin in all 7 cases. In the remaining 6 infants clinical and haematological investigations supported a diagnosis of intrinsic bleeding, and the haemoglobin–alkali test gave a positive reaction for foetal blood.

If further experience confirms these findings it may be possible to omit the more elaborate blood and radiological examinations hitherto employed, especially in cases in which the stools give a positive reaction for the adult type of haemoglobin. *R. M. Todd*

CLINICAL PAEDIATRICS

495. **Hypernatremia in Infants. An Evaluation of the Clinical and Biochemical Findings Accompanying This State**

L. Finberg and H. E. Harrison. *Pediatrics* [*Pediatrics*] **16**, 1–14, July, 1955. 5 figs., 19 refs.

A study was made at Baltimore City Hospitals (Johns Hopkins University), Baltimore, of 88 infants under 2 years of age with hypernatraemia (serum sodium concentration over 150 mEq. per litre), of whom 69 were admitted with diarrhoea, and of 205 other infants also admitted with diarrhoea in whom the serum sodium level was not raised. The hypernatraemic infants all had a history of greatly curtailed water intake during the 24 hours or more before admission, and in some fever and hyperventilation were contributory factors. Only about half of them, however, were visibly dehydrated on first examination.

Of the 69 hypernatraemic infants with diarrhoea, 8 (11·6%) died, whereas only 4 (2%) of the other 205 infants died; the difference is statistically significant ($p<0·01$). The age distribution was similar in the two groups, about 65% of each being under 5 months of age, but there was a larger proportion of premature infants in the hypernatraemic group (38%) than in the other (24%).

Involvement of the central nervous system occurred in two-thirds of the hypernatraemic infants. The protein level in the cerebrospinal fluid was greater than 50 mg. per 100 ml. in 30 out of 32 hypernatraemic infants (94%) and in 9 out of 22 of the non-hypernatraemic infants (41%). The severity of the neurological symptoms was not related to the degree of hypernatraemia. The plasma bicarbonate concentration was less than 15 mEq. per litre in 58 and more than 27 mEq. per litre in 7 of the 88 hypernatraemic infants. In some cases the serum potassium level was low despite a raised blood urea content; in these cases there was no significant correlation between serum potassium and plasma bicarbonate levels. Of 38 hypernatraemic infants, the serum calcium concentration was less than 9 mg. per 100 ml. in 28, and less than 7 mg. per 100 ml. in 7, whereas of 65 of the non-hypernatraemic infants only 3 had a serum calcium level below 9 mg. and only one below 7 mg. per 100 ml. There was no corresponding hyperphosphataemia in any of these cases, nor was the blood calcium level significantly correlated with the bicarbonate level.

A balance study carried out on one patient during the first 24 hours of rehydration with 225 ml. of water per kg. body weight containing 15 mEq. of sodium per litre (the recommended treatment), suggested that there was no shift of sodium into or out of the intracellular compartment during the treatment. About two-thirds of the water retained was added to the intracellular compartment. The authors stress the importance of recognizing this particular type of dehydration, which requires special treatment. *M. Lubran*

496. **The Leucoses of Very Young Infants.** (Les leucoses des trés jeunes enfants)

J. Bernard, G. Mathé, J. C. Delorme, and O. Barnoud. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 470–502, 1955. 9 figs., bibliography.

The authors describe, from the Hôpital Hérold, Paris, 10 cases of leukaemia in very young children, one newborn and all under the age of 6 months. A review of some 80 cases previously published in the literature confirms the widely held view that the disease is commoner in firstborn children. The symptomatology is similar to that of other acute leukaemias, but the frequency of the various signs is rather different. For example, bone involvement is not common and the anaemia is often not severe, whereas thrombocytopenia is frequent, as is also a high leucocyte count; leucopenic forms are extremely rare. The haemogram rarely presents a hiatus leukaemicus, but the blood picture is extremely primitive. There are usually haemorrhages, splenomegaly, and fever.

Leukaemias in very young infants are often associated with congenital abnormalities, such as cardiac malformation or mongolism; there were 3 such cases in the present series.

[This paper is worthy of study in the original, since it contains a mass of information which is difficult to find elsewhere and a useful bibliography.] *A. Piney*

497. ***Hemophilus influenzae* Type B Pneumonia**

W. L. Nyhan, D. R. Rectanus, and M. D. Fousek. *Pediatrics* [*Pediatrics*] **16**, 31–42, July, 1955. 6 figs., 31 refs.

The authors report 5 cases of lobar pneumonia due to *Haemophilus influenzae* Type B, 4 in children under 5 and one in an adult aged 62, from the records of the Grace–New Haven Community Hospital (Yale University School of Medicine) over a period of approximately 15 years. They agree with previous authors that the best way of isolating the infecting organism in such cases is by routine blood culture in the early stages of the disease, before the start of chemotherapy. Clinically, the physical signs of the condition are those of a lobar or segmental consolidation of the type usually associated with pneumococcal pneumonia, from which it may be distinguished by an extreme degree of toxicity and prostration. However, as was demonstrated in 2 of the authors' cases, this is not always present—in fact one of these patients was regarded at first as having a mild upper

respiratory infection and was treated symptomatically as an out-patient, with a fatal issue 4 days later, the diagnosis being established by culture from lung tissue at necropsy. The other 4 patients recovered completely, the children within 1 or 2 weeks and the adult within 4 weeks of onset. Two of the children responded well to treatment with sulphapyridine and sulphathiazole alone, and the other 2 patients to treatment with penicillin, to which streptomycin was added later after the infecting organism had been recognized.

The authors stress that if penicillin is used in treating lobar pneumonia before a bacteriological diagnosis has been made, " the role of the influenza bacillus . . . may go unrecognized. These considerations assume clinical importance as regards the rather aggressive and prolonged therapy indicated for *H. influenzae* infections, as well as the possibilities of complicating empyema or meningitis ". In the light of present knowledge they recommend [quite rightly in the abstracter's opinion] treatment with a combination of two antibacterial drugs, either streptomycin and a sulphonamide or chloramphenicol and a sulphonamide. They favour the latter combination of drugs.

[Meningitis due to *H. influenzae* Type B did not seem to be recognized in Great Britain until a number of American publications had drawn attention to it, and it seems quite probable that this story will be repeated all over again with the pneumonia. *H. influenzae* pneumonia might well be diagnosed more frequently in Britain if blood culture was more generally used as a routine diagnostic procedure in pneumonia.]

K. Zinnemann

498. **The Physical Effects of ACTH and Cortisone in Children.** (Effets psychiques de l'ACTH et de la cortisone chez l'enfant)

P. Mozziconacci, C. Koupernik, and D. Lyard. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **71**, 531–539, May 13, 1955.

In a study of 57 children under treatment with cortisone at the Clinique Médicale des Enfants, Paris, for various illnesses side-effects attributable to the drug were observed in 46. In all but 2 of these cases the reactions were minor, consisting of morbidly increased appetite, sleeplessness, restlessness occasionally amounting almost to hypomania, and states of temporary anxiety and depression. The two severe upsets occurred in a 7-year-old boy who developed a hallucinated confusional state and a 5-year-old girl who went into convulsions and coma from which she emerged in a state of idiocy. [The role of cortisone in the aetiology of this second case is speculative.]

The authors emphasize that reactions are most prone to occur at the beginning and end of treatment. Most of the patients showing reactions also showed signs of hypercorticism, and this may be an indicator of susceptibility. An abnormal electroencephalogram did not seem to be a pointer, but a neuropathic family history was often elicited. The authors do not consider that minor manifestations need be a contraindication to use of cortisone when this is necessary, but suggest that in such cases the dose should be reduced or treatment given intermittently.

M. E. MacGregor

499. **Gastroenteritis in Infants Due to Infection with *Escherichia coli*.** (Les infections du nourrisson à *Escherichia coli* de gastro-entérite infantile)

J. Marie, J. Salet, L. Le Minor, E. Eliachar, and G. Payet. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 2232–2242, June 22, 1955. 7 figs., 35 refs.

The authors report the results of an intensive study of infantile gastroenteritis as seen at the Hôpital des Enfants-Malades, Paris, in 85 infants aged from 10 days to 2 years, not one of whom had been entirely breast-fed; in 24 cases the infection was apparently contracted in hospital. A thorough search for the responsible pathogen in likely vehicles was carried out in an effort to determine the mode of spread of the infection, with the following results: (1) in cow's milk and dried milk—results all negative; (2) in dust from the infected cubicles, cots, bed linen, and hand basins—of 22 cultures, 16 were negative and 6 positive for *Escherichia coli* O111; (3) on the hands of the nursing and medical staff—all negative; (4) in the throats of the affected infants—in 5 cases the same organism was isolated as was present in the stools. The authors believe that the infection reaches the infant's mouth either directly through infected articles or indirectly through the air. During one outbreak they found that even the strictest precautions did not prevent cross-infection.

The clinical features were the classic ones, namely, sudden onset, frequent watery stools with a foetid odour, rapid loss of fluid and electrolytes, fever, and vomiting. The general condition was variable, 23 infants showing signs of toxaemia, from which 7 died [the authors rightly stressing the seriousness of this initial toxic state], while 32 had severe attacks but no toxic symptoms and the remainder had mild attacks. There were 21 cases of relapse, in all of which pathogenic *E. coli* reappeared in the stools, both during and after antibiotic treatment. The prognosis was worse in the younger infants, especially those under 6 months of age, and was also worse in infections due to Strain O111. This strain was found to be more toxic than either Strain O55 or O26 and was also responsible for the majority of the hospital cross-infections. In all, 80 cases were treated with antibiotics, with the death of 7 infants infected with O111 and of one infected with O55; in 5 mild cases no antibiotic treatment was given.

Blood cultures were performed on 20 occasions with negative results, and culture of the urine showed no specific *E. coli* to be present. The cerebrospinal fluid was normal in all [number not stated] subjected to lumbar puncture. Otitis media was found 11 times, as a complication but not as a cause of the disease, but there was no case of mastoiditis.

Samples of stool were taken for culture on admission and repeated 2 or 3 times a week. Strain O111 was isolated in 62 cases, O55 in 13 cases, and O26 in 10 cases. There was no definite relationship between the clinical condition and the finding of a positive culture, and the authors suggest the possible existence of healthy carriers.

Phage-typing of the strains isolated showed a multiplicity of phage-types for each serotype. Treatment with the specific bacteriophage gave no appreciable results. Serological tests for agglutinins were carried out 10 days or more after the onset of the illness. Out of 70 patients tested, 58 showed specific agglutinins for the infecting organism in titres of 1 in 10 to 1 in 160, but 12 were completely negative. The power of producing antibodies, according to the authors' findings, does not depend on the infecting type, the severity of the illness, the antibiotic given, or the age of the patient, but appears to depend rather on some factor special to the individual. Control tests for specific agglutinins carried out on 14 healthy infants were all negative. Sheep erythrocytes sensitized with the antigens of the infecting strain of *E. coli* were agglutinated by the patient's serum, this haemagglutination in some cases being demonstrated before the bacterial agglutination.

The protective power of the patient's serum against infection was studied in 12 cases by inoculating embryonated eggs with a constant dose of serum to which increasing quantities of organisms, from 200 to 2,000 per ml., had been added. The protective power of the serum appeared after the 5th day of the illness, was greater in the older patients, and was independent of the treatment adopted. The protective power of the serum did not always run parallel with the serum agglutinin titre.

L. J. M. Laurent

500. **Preventive and Curative Treatment of Outbreaks of Gastroenteritis Due to Infection with *Escherichia coli*.** (Traitement curatif et préventif des infections de crèches déterminées par les *Escherichia coli* de gastro-entérite infantile)

J. Marie, J. Salet, L. Le Minor, M. Berkman, and G. Payet. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 2243–2249, June 22, 1955. 9 refs.

The authors outline the methods adopted at the Hôpital des Enfants-Malades, Paris, for the treatment of gastroenteritis in infants. This consists mainly in careful diet and rehydration and the oral administration of an antibiotic effective against the infecting type of *Escherichia coli*. Pending the result of sensitivity tests they employ aureomycin, oxytetracycline, or chloramphenicol indiscriminately in identical doses, later changing the antibiotic if necessary according to the result of the tests. Until recently they preferred chloramphenicol, which they gave in a dosage of 50 mg. per kg. body weight 5 or 6 times daily for 5 or 6 days, short courses and moderate doses being preferred to avoid side-effects. In severe and toxic cases they supplemented the chloramphenicol with penicillin and streptomycin intramuscularly. For the last 6 months, however, they have used neomycin in the place of chloramphenicol with much better results. When given intramuscularly this antibiotic is toxic to the kidney and the labyrinth, but given orally it is passed with the faeces practically unabsorbed. In 15 recent cases, all due to infection with *E. coli* Strain O111, 50 mg. of neomycin per kg. body weight was given daily for 6 days, in addition to the usual symptomatic treatment. The drug was well tolerated and no toxic effects were observed. All the infants recovered rapidly and on discharge from hospital the stool culture was negative.

The authors review the various unsuccessful attempts made in the past to prevent or arrest outbreaks of gastroenteritis in hospital nurseries. They decided to try the effect of chemoprophylaxis with "neo-bacitracin", a combination of neomycin and bacitracin in which the two drugs have some synergistic action. A daily dose of 25 mg. of neomycin and 2,500 units of bacitracin was given to every infant admitted, irrespective of age and weight, and for the entire duration of his stay in hospital. The experiment was carried out for a period of 2 months in a nursery where gastroenteritis due to Strain O111 had been rife and endemic for a long time. (They did not consider it to be justifiable to set up a control series.) With 2 exceptions, 36 infants who were continuously exposed to the risks of infection remained well and with negative stools during the 2 months, and there were no further cases. Clinical and laboratory investigations showed no toxic effects from the chemoprophylaxis.

L. J. M. Laurent

501. **Follow-up Investigation of Children with Ulcerative Colitis. With Special Reference to Indications for Surgical Therapy.** [In English]

R. Lagercrantz. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **44**, 302–317, July, 1955. 1 fig., 28 refs.

This paper from Karolinska Sjukhuset, Stockholm, provides a detailed study of 137 patients who developed ulcerative colitis before the age of 15 years, and who have been followed up for 2 to 26 years, in which the effect on the course of the disease of various methods of treatment is analysed. Chemotherapy appeared to have no effect on the long-term prognosis, but psychotherapy was found to be useful, although it did not directly influence the pathological process. Of 19 patients who died, the cause of death was ulcerative colitis or its complications in 17; 8·8% of the survivors were severely incapacitated, while carcinoma of the colon developed in 4·4% of the whole series. In view of these findings, and because in 5 cases where combined ileostomy and colectomy were carried out good results were obtained, a plea is made for the more frequent and earlier use of surgery in the treatment of this incapacitating disease.

I. A. B. Cathie

502. **Magnesia and Alkaline Carminatives in Infancy**

R. D. G. Creery. *British Medical Journal* [*Brit. med. J.*] **2**, 178–179, July 16, 1955. 10 refs.

During investigations into the aetiology of idiopathic hypercalcaemia in infants a history of prolonged ingestion of magnesia or other alkaline mixtures was frequently obtained. Although it was concluded that this finding had no direct bearing on the occurrence of the disease, it emphasized how commonly magnesia and alkaline carminative mixtures are given to small children. To gain more information on this point a survey was made of 200 apparently healthy children between the ages of 6 months and 3 years attending a B.C.G. vaccination clinic at the Royal Belfast Hospital for Sick Children.

No less than 92% were found to have received an alkaline mixture at some time; 79% had been given occasional or regular doses of magnesia, usually for so-called "regulation of the bowels" but often for very vague reasons; and 66·5% had been given carminatives, usually for "wind". Of the two types of preparation, the carminatives commonly used are much less alkaline than magnesia, but in some cases large doses had been given, often for prolonged periods. Although no definite harm was detected, it is considered that such therapy is both "meddlesome and unnecessary", and that the habit should be discouraged. Usually the drugs were given by the parents on their own initiative or on the advice of relatives; but a number of parents stated that they had been advised to give these mixtures by doctors, nurses, or chemists. *A. Paton*

503. **Intestinal Obstruction. I. Causes and Management in Infants and Children**
H. WILSON, J. D. HARDY, and J. L. FARRINGER. *Annals of Surgery* [*Ann. Surg.*] **141**, 778–791, June, 1955. 14 figs., 12 refs.

The authors review the causes of obstruction of the gastro-intestinal tract in early life, as seen in 110 cases admitted to the John Gaston Hospital (University of Tennessee), Memphis, during the 5-year period 1949–53 and discuss their methods of treatment and the results. The most common causes were congenital hypertrophic pyloric stenosis, strangulated inguinal hernia, and intussusception, which together accounted for 74 of the cases.

The 17 cases of congenital pyloric stenosis, the signs and symptoms of which are described, were all operated on with good results; this is attributed largely to early diagnosis and careful attention to maintenance of body fluids. For strangulated inguinal hernia, of which there were 41 cases in patients whose average age was 2 years, immediate operation is recommended; the authors employ a skin-crease incision, subcuticular stitches, and a colloidin dressing, and the child is allowed no napkins for several days. In the 16 cases of ileocaecal intussusception (average age of patients 6 months), the intussusception was reduced by operation in preference to the barium-enema technique; when gangrene was present the bowel was resected, and a case of colonocolic intussusception due to peristaltic traction on a polyp was encountered, in which local excision of the polyp was required in addition to reduction; there were 2 deaths in this group. Of the 6 cases of congenital atresia in the series the duodenum was affected in 3. If the atresia was below the duodenal papilla a gastroduodenostomy was performed; if above that level gastro-jejunostomy was preferred. The authors advise that multiple sites of atresia should always be expected and tested for by "milking" gas along the bowel or injecting saline. The results of surgery in this condition were disappointing.

Other less frequent causes of intestinal obstruction encountered were anomalies of rotation of the gut and volvulus (6 cases), adhesions (8), imperforate anus (6), annular pancreas (4), and Meckel's diverticulum (2 cases). The radiological findings and treatment of these conditions are detailed and discussed, and a useful table is given of points likely to be of value in diagnosis, including the character of the vomitus or faeces and the most usual age at which the various types of intestinal obstruction are likely to be met. *Charles Nicholas*

504. **The Prepuberal Diagnosis of Ovarian Agenesis and its Relationship to Status Bonnevie–Ullrich**
J. W. OBERMAN. *Journal of Pediatrics* [*J. Pediat.*] **47**, 48–59, July, 1955. 6 figs., 19 refs.

A 27-month-old female infant with the Bonnevie–Ullrich syndrome and a female child of 11 years with Turner's syndrome have been studied at the Children's Hospital, Washington, D.C. The Bonnevie–Ullrich syndrome is usually recognized before the onset of puberty, and the four main features are pterygium colli, lymphangiectatic oedema of the extremities, mental retardation, and cutis laxa; on the other hand Turner's syndrome, manifested by the triad of sexual infantilism, pterygium colli, and cubitus valgus, is not usually recognized before puberty. Many other clinical features common to both these syndromes may also be present. The author stresses their essential unity and suggests that the name Bonnevie–Ullrich–Turner syndrome be applied to both of them. It is thought that such a concept will lead to earlier diagnosis and better appreciation of the probable future course of development of the child in such cases. *R. M. Todd*

505. **Problems in the Classification of Cerebral Palsy in Childhood**
C. L. BALF and T. T. S. INGRAM. *British Medical Journal* [*Brit. med. J.*] **2**, 163–166, July 16, 1955. 28 refs.

Feeling the need for a standard terminology for use in cases of cerebral palsy, the authors, writing from the University of Edinburgh, put forward a classification based on well-established terms used in adult neurology. The categories distinguished are: hemiplegia, double hemiplegia, diplegia, ataxic diplegia, ataxia, and dyskinesia. [The first two need no comment except that cases in which athetoid movements are associated with hemiplegia are not differentiated, cases of hemiplegia being subdivided only according to severity. Though this may hardly be justified anatomically, it serves a useful purpose in keeping separate the large group of cases of spastic paresis with athetoid movements from the much smaller group of cases of pure athetosis.] The term diplegia is used to describe "a more or less symmetrical paresis of cerebral origin"; cases with involvement of the arms are included provided that the legs are more severely affected, in contradistinction to double hemiplegia. The authors describe the stages of evolution in diplegia—poverty of movement and hypotonia in the early weeks and phasic opisthotonus in the next few months, followed by a phase of rigidity in which the deep reflexes may be difficult to elicit and a flexor plantar response may even be present, with the final appearance of true spasticity in the adult sense of the word. A history of a hypotonic phase is obtained in about 40% of cases, and of a dystonic phase in 50%.

Cases of ataxic diplegia, or the diataxia of Ramsay Hunt, form about 6% of all cases of cerebral palsy. Though ataxia is the prominent feature, some increase in extensor tone is common, though there is no adductor spasm. These cases do not pass through a dystonic phase and are rarely attributable to anoxia, and there is sometimes a positive family history. The spasticity is usually mild, distinguishing these cases from the equally uncommon cases of pure ataxia.

Amongst the conditions falling into the category of dyskinesia are those in which torsion dystonic, choreiform, or athetotic movements occur in the absence of hemiplegia, double hemiplegia, or diplegia. Such cases form only 8% of the total. [The use of these three established terms is preferable to the 13 or more subdivisions of athetosis which have confused the literature in the past few years.] *J. Foley*

506. Infantile Spastic Hemiplegia

M. A. PERLSTEIN and P. N. HOOD. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **34**, 391–407, June, 1955. 21 refs.

This is a study of 334 spastic hemiplegics, ranging in age from less than a year to more than 20 years, with a mean age of 6·5 years. From statistical analysis of these records, the following facts emerge concerning infantile spastic hemiplegics.

There were more right than left spastic hemiplegics in the ratio of 5 : 4. The lefts and rights were distributed randomly between the congenital and postnatally acquired, the male and female and those with or without seizures. There was no significant difference in the intelligence of the lefts vs. rights, nor in the age of acquiring speech. The only other significant difference between the lefts and rights, was the even greater proportion of rights (2 : 1) in the congenital cases having birth weights of 8 pounds [3·6 kg.] and above.

Spastic hemiplegia occurred more often in males than in females (4 : 3); however, sex was not related to any of the other variables in this series, including birth weight. Negroes did not differ from whites in this series, with the exception of their greater incidence in the postnatally acquired and in the seizure groups. These differences were thought to be the result of socio-economic factors, rather than racial factors.

Whereas postnatally acquired cases account for about a tenth of the total cerebral palsy population, they made up approximately a third of the present series. The time of onset of hemiplegia was unrelated to race, sex, side of involvement or intelligence. However, an earlier age of walking and talking was noted in the postnatally acquired cases whose onset of cerebral palsy predated the acquisition of these skills, as compared to the congenital hemiplegics.

The incidence of seizures in this series was significantly higher than that reported for all types of brain injury for mixed spastic groups, and for most other series of spastic hemiplegics. Seizures in this series were significantly more prevalent in the acquired and in the mentally defective cases; moreover, they showed a significantly lower mean I.Q. score. Seizure also delayed, to a significant degree, the onset of walking and talking words but were not related to the acquisition of sentences nor to birth weight.

Spastic hemiplegics were approximately 20 I.Q. points retarded from normal children. Although the mean I.Q. scores did not differ significantly, there was a significantly greater number of mental defectives below than above the age of six; however, there was no relation between age and intelligence when cases were grouped in one-year intervals. The mentally defective group walked and talked later than did the educable group. Those of I.Q. between 90–110 differed only slightly from normal children in walking and talking.

Spastic hemiplegics were 0·7 lb. [0·3 kg.] lighter than normal infants, the mean birth weight being 6·4 lb. [2·9 kg.]. The proportion of prematures and abnormally heavy birth weights was significantly greater in spastic hemiplegics than in normals.

A consideration of some of the correlational aspects of the data revealed a strong relationship between the ages of talking words and talking sentences, less marked relationships between walking and talking, and negligible relationships between birth weight and all other variables. There was a substantial relationship between the age of walking and the age of the onset of the spastic hemiplegia in the acquired cases; other variables were not related to the age of onset in acquired hemiplegia.—[Authors' summary.]

507. Congenital Dermal Sinuses in Children. Their Relation to Pilonidal Sinuses

J. C. HAWORTH and R. B. ZACHARY. *Lancet* [*Lancet*] **2**, 10–14, July 2, 1955. 6 figs., 32 refs.

The authors describe 18 cases of congenital dermal sinus of the sacro-coccygeal region seen at the Children's Hospital, Sheffield. In 3 the sinus communicated with the central nervous system and meningitis following infection developed in 2 of them. In 2 of the other 15 cases there was local infection of the sinus, which in one case travelled upwards apparently in the extradural tissue—the sinus did not communicate with the meninges—and caused formation of a fatal extradural abscess; in the other case the infection was local and resulted in the formation of an early pilonidal sinus. In all of these 15 cases the sinus was situated over the coccyx, and in those dissected out at operation or necropsy the epithelial tube was found to be connected by a fibrous band to the tip of the coccyx. Two of the children with blind sinuses also had spina bifida, and one had a meningo-myelocele. Among 500 children examined at the hospital a congenital dermal sinus was found in 7 cases (1·4%), and deep dimples in the coccygeal region in a further 2·8%.

The origin of so-called "pilonidal sinus" is then discussed. The authors advance arguments to show that a pilonidal sinus in the sacrococcygeal area is merely the result of infection of a congenital dermal sinus, with occlusion of the orifice, and that the hair in the sinus grows *in situ*. Congenital dermal sinuses should be excised because of the danger of local infection, with its liability to spread into the central nervous system. *E. H. Johnson*

Medical Genetics

508. **Mongolism in Twins. Its Bearing upon the Question of the Etiology of Mongolism**
A. FRIEDMAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **90**, 43–50, July, 1955. 28 refs.

The author reports three instances of mongolism in association with twinning which were studied at the Cook County Hospital, Chicago. The first pair, who were negroes, consisted of a mongol boy and a normal twin sister. The second pair, also negroes, consisted of a mongol boy whose twin brother had died at the age of 28 days; there was no suggestion that the latter was also a mongol. The third pair were white and consisted of a mongol boy and a normal twin sister. The first and third pairs were clearly dizygous, because the twins differed in sex, but the type of twinning in the second pair could not be determined.

The author summarizes previous work on mongolism in twins, his own cases bringing the total of those reported in the literature to 113; in 42 cases the pair was certainly dizygous, the twins being of unlike sex, and in all these only one of the two was a mongol. In all the 21 instances in which both twins were affected they were of the same sex; in 10 of these the twins were probably monozygous, in 8 the type of twinning was uncertain, and in 3 the twins were probably dizygous. He concludes that no definite conclusions can yet be drawn concerning the aetiology of mongolism on the basis of twin studies, the number of cases recorded being inadequate, the diagnosis of zygosis uncertain, and the key cases—that is, one or more discordant monozygotic pairs or one or more concordant pairs of unlike sex—being as yet missing from the literature. *C. O. Carter*

509. **The Inheritance of Porphyria**
G. DEAN and H. D. BARNES. *British Medical Journal* [*Brit. med. J.*] **2**, 89–94, July 9, 1955. 1 fig., 7 refs.

The genealogies were traced of 13 South African families in which there were 236 members (121 males and 115 females) with clinical manifestations of acute porphyria, chronic cutaneous porphyria, or symptomless porphyria. From a review of the clinical and biochemical findings the authors assert that these are different manifestations of the same genetically-determined disorder, and that one type may change into another. Sex differences in symptomatology were pronounced; affected males had a sensitive, easily blistered skin, but were otherwise generally well except when administration of barbiturates precipitated an acute attack; affected females had less marked cutaneous manifestations, but were often more emotionally unstable than males and therefore especially prone to crises of abdominal pain and peripheral neuritis following barbiturate sedation.

The authors discuss at some length the occurrence of the disorder in one large family (the pedigree is reproduced) in which 60 members out of 446 in 4 generations were affected. Specimens of urine from all living members of this family were examined. Of the adults with one affected parent 48% were affected (24 out of 41 males and 36 out of 84 females). For all the 13 families the figures were 51·3% of males and 48·7% of females, so that the results are in accord with the requirements for postulating inheritance by an autosomal dominant gene. Detailed histories of 11 of the cases of acute porphyria in the one family are presented.

R. H. Cawley

510. **Parental Age and Mutation**
L. S. PENROSE. *Lancet* [*Lancet*] **2**, 312–313, Aug. 13, 1955. 23 refs.

Certain human malformations and diseases are believed to result from fresh mutation of single genes in cells in the germ line. The author suggests that the most likely causes of such mutations are: (1) failure to copy the gene accurately at cell division; (2) irradiation from natural sources, such as cosmic rays and radioactive substances; and (3) chemical mutagenic agents, possibly toxic by-products of normal metabolism. Theoretically, the incidence of defects associated with mutations of Type 1 would be expected to increase markedly with increasing paternal age and to have no strong relation to maternal age, since there are many more cell divisions in the male than in the female germ line. The incidence of those due to Type-2 mutations would be expected to increase with both maternal and paternal age, being dependent on the total exposure of the germ cells to irradiation irrespective of the number of cell divisions. The incidence of defects due to mutations of Type 3, on the other hand, might possibly be expected to increase with maternal rather than paternal age, toxic substances being more likely to accumulate in the cytoplasm of ova than of spermatozoa. The mean ages of the fathers and mothers of children showing particular traits, and the differences between these means, should thus provide critical indices of the types of mutation responsible for them.

Estimates of mean parental ages calculated from data in the literature relating to various congenital malformations are tabulated, and the author stresses the significance of the findings with regard to achondroplasia, a sporadically-occurring disorder of which the incidence appears to be closely related to paternal age only; this is regarded as providing support for the hypothesis that a fresh gene mutation of Type 1 is responsible. On the other hand the observed increase in the incidence of mongolism with maternal age is held to be much greater than could be expected in the case of a mutation of Type 3, suggesting a different type of causation. The need for a more accurate and detailed inquiry into the incidence of malformations in relation to the ages of the parents is emphasized.

R. H. Cawley

Public Health

511. **The Recent Pattern of Acute Poliomyelitis in England and Wales**
W. J. MARTIN. *Medical Officer* [*Med. Offr*] **94**, 19–21, July 8, 1955.

Reviewing statistics for acute poliomyelitis in England and Wales for the 5-year period 1950–54, the author finds that these do not support the view that when the disease is especially prevalent proportionately more cases of the non-paralytic form are notified. During these 5 years no definite relationship was apparent between the incidence of the disease and the proportion of paralytic cases. On the other hand over the whole 5-year period notifications of non-paralytic poliomyelitis were highest in the third quarter of each year —that is, when the incidence of the disease was highest. Although the incidence of poliomyelitis was much higher in the fourth quarter than in the second, the number of cases of non-paralytic disease was slightly lower in the former. This trend was not consistently reproduced in each year. The proportion of paralytic cases to total cases was highest in infancy, declined steadily until age 10 to 14 years, and then rose; the author suggests that the high proportion of paralytic cases in childhood may be attributed in part to failure to recognize the non-paralytic form at an early age. At all ages, and for both paralytic and non-paralytic disease, the ratio of affected males to affected females was 4 : 1.

The proportion of paralytic cases to total cases varied in the different regions in the 4 years for which information was available, the proportion in the East and West Ridings of Yorkshire and in the North-Western and Wales II Regions being higher than in England and Wales as a whole, but only in Wales I was the proportion below the average in each of the 4 years. The biggest outbreaks occurred in the Northern, Midland, and South-Western Regions. In childhood, females had a slightly higher chance than males of surviving an acute attack of poliomyelitis, but at age 25 and over the fatality rate in males was 40% higher than that in females; in the Northern and North-Western Regions mortality among men at age 25 and over was double that among women.

R. G. Meyer

512. **Incidence of Retrolental Fibroplasia in England and Wales in 1951**
J. T. BOYD and K. M. HIRST. *British Medical Journal* [*Brit. med. J.*] **2**, 83–85, July 9, 1955. 2 refs.

In 1952 the authors investigated on behalf of the Ministry of Health the incidence of retrolental fibroplasia in England and Wales among premature babies born the previous year (1951) who weighed not more than 4 lb. 6 oz. (2,000 g.) at birth and who had survived for at least 2 months, that is, long enough for evidence of retrolental fibroplasia to become apparent. The relevant information was obtained mainly through the local health authorities, the health visitors carrying out the first inquiry, while in doubtful cases the family doctor and an ophthalmologist were consulted.

Among the 6,926 infants in the series the over-all incidence of retrolental fibroplasia was 1·83%. Analysis of incidence by birth weight showed that the percentage increased with decreasing birth weight; for example, in those under 2 lb. 4 oz. (1,000 g.) at birth it was 15·3%, whereas in those weighing between 3 lb. 14 oz. and 4 lb. 6 oz. (1,750 and 2,000 g.) it was only 0·2%. Every one of the 127 cases of retrolental fibroplasia occurred among the 6,042 infants born in hospital or transferred there within 2 months of birth, none of the 797 born at home developing the disease; this fact supports the view that retrolental fibroplasia is "associated with some factor connected with hospitalization". The total incidence among male infants was higher (2·7%) than in females (1·6%), the difference being statistically significant. It is suggested that this may well be due to the fact that male babies are less mature than females of the same weight. To check this, two groups of infants at similar levels of maturity, consisting of the first 500 infants of each sex in ascending order of birth weight (males up to 3 lb. 5 oz. (1,500 g.) and females up to 3 lb. 2 oz. (1,420 g.)) were compared. The number of cases of retrolental fibroplasia in the two groups was respectively 47 and 38—this difference not being statistically significant. There was no increased incidence in infants of multiple births.

The three highest incidence rates occurred in north-west England, Wales, and south-east England, and the three lowest in the Midlands, the East and West Ridings of Yorkshire, and northern England.

Elaine M. Osborne

513. **Vital Statistics of the County of London in the Years 1901 to 1951**
W. J. MARTIN. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **9**, 126–134, July, 1955. 1 fig., 6 refs.

Between 1901 and 1931 the population of the County of London was approximately stationary. Between 1931 and 1951 it fell by over a million, and in 7 of the 28 boroughs the population in 1951 was only about half that in 1931. The result of these changes was a great reduction in the proportion of persons living in overcrowded conditions. From 1901 to 1931 the proportion of the population living more than two persons to a room was between 1 in 6 and 1 in 8; by 1951 it had fallen to 1 in 40. From 1901 to 1931 about 3% of the population of London was foreign-born; in 1951 the figure was 5% for the County, and over 10% in 4 boroughs—Hampstead (16%), Kensington (12%), Paddington (10%), and St. Marylebone (12%).

The downward trend of the death rate during the 20th Century has been remarkably similar in the London boroughs, so that the boroughs with the highest and

lowest rates in 1911–13 were in the same relative position in 1950–52. The fall has, however, been larger in the boroughs where the rate previously was highest so that the actual and relative range of the death rates between London boroughs in 1950–52 was somewhat smaller than in 1911–13. The general death rate (standardized) is still significantly correlated with the indices of socio-economic status (persons per room, and percentage in Social Classes IV and V).

The birth rate followed a trend similar to that of the death rate, and, generally, the relative level of the birth rate of a borough, high or low, has remained the same throughout the period. With the exception of the percentage of the population living more than two to a room, the correlations between the birth rate and the socio-economic indices have changed very little.

The very large fall in infant mortality in the London boroughs has been relatively greater in those boroughs where the initial level was highest. In 1911–13 and 1920–22, infant mortality was significantly correlated with the percentage of occupied males in Social Classes IV and V and with the two measures of overcrowding. In 1930–32 the correlations between infant mortality and overcrowding were reduced but still significant, while the percentage of occupied males in Social Classes IV and V was not significantly correlated with infant mortality. In 1950–52 the correlations between infant mortality and the three indices were not significant. The lack of correlation in 1950–52 was partly due to the increasing contribution made by neonatal mortality, and partly to the fact that the relationship is no longer demonstrable in the smaller boroughs although it still exists in the largest boroughs. If the neonatal component is excluded, the correlation of infant mortality for the first year of life is significant in 1950–52 for each of the three socio-economic indices. The successful efforts to reduce overcrowding have lessened the sensitivity of this index of socio-economic conditions. In 1911 the percentage of persons living more than two to a room ranged from 3·9 to 39·8 in the London boroughs, while in 1951 the range was only from 1·3 to 4·6; thus this index of overcrowding was no longer a measure of either the vital-statistical or socio-economic differences between the London boroughs in 1950–52.—[Author's summary.]

514. The Sterilisation of Blankets with Cetyl Trimethylamine Bromide

R. BLOWERS and K. R. WALLACE. *Lancet* [*Lancet*] 1, 1250–1252, June 18, 1955. 3 figs., 8 refs.

Blankets are an important reservoir of pathogenic organisms because the usual method of laundering by low-temperature wash does not sterilize them. The use of quaternary ammonium compounds in laundering has been suggested by several workers, who have found that the bacterial count on blankets after such treatment is very low. Cetyl pyridinium bromide ("fixanol C") has also been tried, but objections to this substance are that it has an unpleasant odour, does not dissolve easily, and stains the blankets.

The present authors have experimented with cetyl trimethylamine bromide ("cirrasol OD"), an odourless, colourless, cationic, surface-active agent which dissolves easily in water. Blankets contaminated in hospital wards were used, and samples were taken by the sweep-plate technique, care being taken to ensure that any residual disinfectant in the samples was neutralized. The blankets were washed in a Manlove and Alliot open-pocket machine fitted with an interrupter gear so that the inner container was rotated intermittently, with consequent less felting and hardening of the blankets than with continuous rotation. After treatment with cirrasol only an occasional organism was isolated from the blankets; the mean colony counts on 78 blankets before and after treatment were 194 and 2·6 respectively. The blankets were normal in appearance and texture and were odourless. To demonstrate that cirrasol remained in the blankets they were shaken over culture plates sown with *Staphylococcus aureus*; after incubation the growth of the staphylococci was completely inhibited.

J. A. Sinclair

515. Serum-sickness and Local Reactions in Tetanus Prophylaxis. A Study of 400 Cases

N. H. MOYNIHAN. *Lancet* [*Lancet*] 2, 264–266, Aug. 6, 1955. 1 fig., 13 refs.

516. Immunization of Babies with Diphtheria–Tetanus–Pertussis Prophylactic

M. BARR, A. T. GLENNY, and N. R. BUTLER. *British Medical Journal* [*Brit. med. J.*] 2, 635–639, Sept. 10, 1955. 8 refs.

This report from the Wellcome Research Laboratories and University College Hospital, London, gives the results of immunization trials in young infants with two triple prophylactics, both of which contained, per ml., 60 Lf of purified diphtheria toxoid, 12 Lf of purified tetanus toxoid, and 4×10^{10} *Haemophilus pertussis*, but which differed in that in one the toxoids were adsorbed on to aluminium hydroxide (the "adsorbed" prophylactic) and in the other no mineral carrier was present (the "fluid" prophylactic). The individual dose in all instances was 0·5 ml., given subcutaneously. Before immunization samples of blood were taken from the umbilical cord to determine the titre of maternally conferred diphtheria antitoxin, and samples were again taken from the babies at about 6 months of age to test the early responses to a course of immunization, further samples being taken still later to test the duration of immunity.

In one group of infants injections of the "adsorbed" prophylactic were given at ages 1, 6, and 14 weeks. In these subjects the diphtheria antitoxin titre fell rapidly in 12 months, but a reinforcing dose was successful in restoring the antitoxin titre to a satisfactory level. The "fluid" prophylactic was given according to three different schemes to three groups of infants, namely, at 6, 12, and 18 weeks, 12, 16, and 20 weeks, and 16, 20, and 24 weeks of age respectively. It was found that the earlier immunization began, the poorer were the antitoxin titres later; but after a reinforcing dose there was little difference in the immunity state in any of the 4 groups. Babies who received the "adsorbed" pro-

phylactic had a much lower titre of tetanus antitoxin at 6 and 12 months than those who were given the "fluid" preparation, but 3 months after a reinforcing dose these differences were no longer present. There was little or no interference with the early response to the diphtheria toxoid, except in infants with a cord-blood titre of 1 unit per ml. or higher who were given the "adsorbed" prophylactic. Satisfactory immunity was established in babies injected with the "fluid" preparation starting at the ages of 16 weeks and 12 weeks, but not in those first injected at 6 weeks. There was good correlation between the diphtheria and tetanus antitoxin titres.

There was a high proportion (53 out of 66) of severe local reactions after injection of the "adsorbed" prophylactic, compared with only 43 out of 379 after the "fluid" preparation. Also, 17 out of 198 infants developed sterile abscesses after inoculation with "adsorbed" but none with the "fluid" prophylactic. A general reaction was uncommon, occurring in only 6% with the "adsorbed" and 9·4% with the "fluid" prophylactic, fever being the most frequent manifestation.

The authors conclude that satisfactory diphtheria and tetanus antitoxin titres can be obtained by the use of the "fluid" combined diphtheria–tetanus–pertussis prophylactic if immunization is started at 12 or 16 weeks of age. The "adsorbed" prophylactic was considered to be less satisfactory, since it caused more local reactions and there was a rapid fall in the diphtheria titre in the second 6 months.

[For more details, the copious figures in the original article should be consulted. It seems not quite justifiable to compare the "adsorbed" preparation with the "fluid" preparation, because they were administered according to different schedules. The response to the whooping-cough vaccine is not considered in this paper.]

John Lorber

517. **Immunization against Diphtheria and Whooping-cough. Combined *v.* Separate Inoculations**

V. SPILLER, J. M. BARNES, L. B. HOLT, and D. E. CULLINGTON. *British Medical Journal* [*Brit. med. J.*] **2**, 639–643, Sept. 10, 1955. 1 fig., 15 refs.

The authors present, from the Public Health Department, Barking, Essex, and the Wright–Fleming Institute, London, an account of a small controlled trial of two different schemes of immunization against diphtheria and whooping-cough in infants between 2 and 5 months of age. The subjects were grouped by random allocation; 79 infants (the "separate group") were given three injections each of 1 ml. of a commercial suspended whooping-cough vaccine followed by two injections of 0·5 ml. of P.T.A.P., all injections being given at monthly intervals, while the other group of 81 infants (the "combined group") received three injections each of 1 ml. of combined whooping-cough–diphtheria (P.T.A.P.) prophylactic, also at monthly intervals. All injections were given subcutaneously. No major reactions were noted in either group.

When the infants were 15 months old, blood samples were taken for estimation of the diphtheria antitoxin and *Haemophilus pertussis* agglutination titres, Schick tests being carried out simultaneously in all cases. The latter gave apparently positive reactions in 9 cases, but 5 of these were found to be pseudo-positive reactions, these 5 being from the separate group. Both methods of inoculation produced very high titres of diphtheria antitoxin in the serum at 15 months, equivalent to a "Schick-positive residue" of 6 for the combined group and of 3 for the separate group per 10,000 inoculated. (The statistical method is explained.) These results were better than those obtained in an earlier trial with 2 doses of A.P.T. (Barr *et al.*, *Lancet*, 1950, **1**, 6; *Abstracts of World Medicine*, 1950, **7**, 563).

The agglutination titres to *H. pertussis* showed a wide range of scatter, but were virtually congruent after both forms of inoculation. The failure rate, defined as the percentage of sera with an agglutination titre less than 1 in 20, was practically the same in both groups, namely, 12·3% (combined) and 10·6% (separate). The number of organisms in the combined vaccine was only half that in the separate vaccine. [No clinical data are available about the protective value of the vaccines against whooping-cough.]

Analysis of the detailed findings showed there was no correlation between the responses of any one individual to the diphtheria toxoid and to the agglutinogen of *H. pertussis* vaccine.

John Lorber

518. **Vaccination against Whooping Cough**

C. O. S. BROOKE. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth (Lond.)*] **14**, 142–144, Sept., 1955. 1 ref.

During an epidemic of whooping-cough in Finsbury, London, in 1953 an attempt was made to determine whether previous vaccination had any marked influence on the incidence or severity of the disease. Altogether 307 children aged 1 year to 12 years had whooping-cough during the epidemic; in 147 of these the attack was severe or moderately severe, with characteristic whoop and vomiting; in more than half of the remainder, who had a slight attack, the diagnosis was confirmed bacteriologically. It was found that 121 of the children had already been vaccinated against whooping-cough and 149 had not; in the remaining 37 the history was uncertain. (The author states that 115 parents could not say whether their children had been immunized against whooping-cough, although they had signed a form of consent which clearly stated the purpose of the injections.)

The investigation revealed that the incidence of whooping-cough was about 60 per 1,000 among the vaccinated children and 37 per 1,000 among the unvaccinated. [The explanation offered for this apparent anomaly is not altogether convincing.] The incidence of severe and moderate attacks was more in line with expectation, being 8 per 1,000 among the vaccinated and 28 per 1,000 among the unvaccinated children. None of the attacks in vaccinated children was severe.

J. Cauchi

519. **The Coxsackie Group of Viruses. Epidemiological Studies.** [In English]

P. POHJANPELTO. *Annales medicinae experimentalis et biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **33**, Suppl. 6, 1–75, 1955. Bibliography.

Industrial Medicine

520. **Pulmonary Disease in Relation to Metallic Oxides**
K. M. A. PERRY. *Lancet* [*Lancet*] **2**, 463–469, Sept. 3, 1955. Bibliography.

The author reviews the present state of knowledge concerning pulmonary diseases caused by metallic oxides (other than silicon dioxide). These include diseases due to inhalation of inert dusts such as those of the oxides of barium, iron, and silver, chemical pneumonia caused by manganese dioxide, and upper respiratory irritation due to the oxides of vanadium and osmium. The acute effects of beryllium on the lung are considered separately from the chronic condition of beryllium sarcoidosis. A form of fibrosis of the lung apparently produced by aluminium oxide and bauxite dust is discussed, and finally the various industrial processes which may produce carcinoma of the lung are briefly mentioned.

C. M. Fletcher

521. **Toxicity of Organophosphorus Compounds. I. Structure–Action Relationships in Laboratory Animals and Man**
J. K. KODAMA, H. H. ANDERSON, M. K. DUNLAP, and C. H. HINE. *Archives of Industrial Health* [*Arch. industr. Hlth*] **11**, 487–493, June, 1955. 27 refs.

This paper from the University of California School of Medicine, San Francisco, is devoted to a review and discussion of the relationship between the structure of the organophosphorus compounds and their toxicity in laboratory animals and in man as found by the authors and as reported in the literature. Because of some confusion in the nomenclature of these compounds the authors have grouped them as follows: (1) phosphorous acid derivatives, phosphites; (2) phosphinic acid derivatives, phosphinates; (3) phosphonic acid derivatives, phosphonates; and (4) phosphoric acid derivatives, phosphates. The toxicity of the organophosphorus compounds is due to one or more of the following four effects.

I. Cholinesterase inhibition. Death may be due to (*a*) a muscarinic effect, causing bronchoconstriction and overstimulation of mucus secretion in the pulmonary tract; (*b*) a nicotinic effect, consisting in stimulation of striated muscle with generalized convulsions, followed by paralysis; (*c*) a central action, manifested at first by stimulation with excitement and disturbance of respiration, followed by depression. The compounds with an anticholinesterase action are almost all derivatives of phosphoric acid, the greatest activity being found in those of the phosphate type which contain a substituted amide and a cyanide as well as an alkoxy substitution. In addition, two phosphonic acid derivatives are proved cholinesterase inhibitors, namely, ethyl *p*-nitrophenyl thionobenzenephosphate (EPN), an insecticide, and "sarin", a possible "antipersonnel agent". A study of 14 phosphites, phosphonites, and phosphonates did not reveal any effective cholinesterase inhibitor among them.

II. Selective degeneration in the central and peripheral nervous system, resulting in various types of paralysis. Three compounds only have been found to possess this action, namely, tri*ortho*tolyl phosphate, di*iso*propylfluorophosphate, and bis-mono*iso*propylaminofluorophosphate ("mipafox").

III. Stimulation of the central nervous system, followed by depression. This action has been noted in poisoning with various phosphinates, phosphites, and phosphonates, as well as phosphates. There is excitement, then ataxia and somnolence; this effect is particularly marked in intoxication with the simple substituted trialkyl phosphates. Generally, large doses are required to produce the syndrome.

IV. Few of these compounds are surface-tissue irritants, but this effect has been noted in some in which one or more of the OH groups remain unsubstituted, or in compounds whose substituted halogen radicals are easily hydrolysed to release a halide acid. The irritation is produced by the presence of hydrogen ions and is not a specific action of the phosphorus atom.

Apart from the three compounds mentioned under II above, and a few cases of accidental ingestion, the incidence of poisoning with these compounds is extremely low and so far they have presented no industrial or public-health problem.

M. A. Dobbin Crawford

522. **Chromate Dermatitis from Chrome Glue and Other Aspects of the Chrome Problem**
G. E. MORRIS. *Archives of Industrial Health* [*Arch. industr. Hlth*] **11**, 368–371, May, 1955. 2 figs., 17 refs.

The manufacture and use of chrome glue should, in the author's opinion, be added to the list of occupations which bear a hazard of chrome dermatitis. The method of making the glue from chrome-tanned leather scrap is described, and 3 cases of chrome dermatitis attributable to contact with it are recorded in detail, one of the patients developing a generalized sensitization dermatitis. In each of these, and in another case of chrome dermatitis of different origin, an acute recurrence resulted from the wearing of leather shoes and was controlled only after the replacement of leather shoes with shoes made of cloth or canvas. A recommendation which the author has found successful in other cases is to wear a plastic lining to the shoe; a plastic bag, as sold to contain food, is suitable, being impermeable to the chemical irritant. The penetrating observation is made that the persistence of chronic chrome dermatitis of the hands is in all probability often due to secondary sensitization of the feet from chrome-tanned leather shoes.

M. A. Dobbin Crawford

Forensic Medicine and Toxicology

523. **The Significance of Foreign Bodies in the Alveoli of the Apparently Drowned**
H. S. HOLDEN and J. W. L. CROSFILL. *Journal of Forensic Medicine* [*J. forensic Med.*] 2, 141–150, July–Sept., 1955. 3 figs., 3 refs.

It is generally accepted that the presence of microscopic particulate matter in the alveoli of the lungs of a body found in water is proof that life was still present when it entered the water, and that inhalation of the fluid medium and particulate matter must have taken place during life.

The authors of the present paper, considering that this assertion was based on flimsy evidence, set out to determine the depth of penetration of finely divided matter into the lungs of drowned rabbits and of rabbits immersed in water after death. When animals were drowned in a suspension of " dicalite ", which is a diatomaceous earth with readily identifiable particles, or of sand it was found, as was to be expected, that the particulate matter reached the alveoli in quantity. When others were killed with " nembutal " (pentobarbitone) and their bodies immersed in a suspension of dicalite for a week particulate matter was found in the alveoli in small amounts in some instances on histological examination, but none was recovered after digestion of the lung tissue in concentrated nitric acid. When rabbits had been drowned in a tidal creek debris was found to be present in the lung; none was found, however, in the lungs of animals previously killed and then immersed in cages in the tidal water.

The authors conclude from their experiments with dicalite that it is possible for solid matter to penetrate into the alveolar spaces of animals killed before immersion in water containing foreign particles, and that the presence of these particles is therefore not proof that life existed at the time of immersion. They are of the opinion that only when a lung section is found to contain a mass of detritus and particulate matter generally disseminated throughout the lung fields, including the marginal alveoli, is it safe to assume that inhalation has taken place after immersion. If only scanty foreign material is present no conclusion can be drawn one way or the other. *Gilbert Forbes*

524. **The Mechanism of Acute Ferrous Sulphate Poisoning**
R. J. K. BROWN and J. D. GRAY. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] 73, 192–197, Aug. 1, 1955. 4 figs., 8 refs.

The authors report a case of acute ferrous sulphate poisoning and the results of an experimental investigation in rabbits which was prompted by clinical observations in the case described. The patient, a 2-year-old boy, swallowed 40 ferrous sulphate tablets and very shortly afterwards passed into a state of semicoma. The clinical course and laboratory findings are described in detail. The following table summarizes the sequence of events in this case.

Time after Poisoning	Clinical Findings
0–12 hours	Period of shock; liver not enlarged
12–24 hours	Apparent improvement; evidence of liver damage
24–48 hours	Condition deteriorating. Reduction in plasma globulin content ; liver enlarged; jaundice present
48–56 hours	Comatose. Liver enlarged; jaundice increased; no protein detected in plasma
72 hours	Improvement apparent; liver function returning
7 days	Improvement continuous; liver still enlarged; plasma globulins low

Treatment included stomach lavage with a 25% solution of sodium bicarbonate immediately after admission to hospital, intravenous infusion of fluids, including casein hydrolysate, and administration of methionine, α-tocopherol, glutamic acid, and penicillin.

Experimentally, 10 rabbits were given intravenously 75 mg. of ferrous sulphate (equivalent to 15 mg. Fe^{++}) in 0·5 ml. of water. During the first 24 hours 4 rabbits died, and the survivors were killed at varying intervals up to 7 days. The main findings were transient saturation of the reticulo-endothelial system with iron, necrosis of the liver, hypoglobulinaemia, and an increase in the blood amino-acid concentration.

The experimental results are discussed in relation to the clinical observations. The authors conclude that ingestion and absorption of large amounts of iron are immediately followed by a period of shock which is caused by the presence of a circulating vasodepressant; " subsequently there is protein loss by destruction and renal discharge, and at the same time protein synthesis is depressed by liver necrosis and the effect of reticulo-endothelial block. The destruction of protein and loss of synthesis lead to a hypoproteinaemia of varying degree by an alteration in amino-acid metabolism ". *P. N. Magee*

525. **The Late Effects of Lead Poisoning**
D. L. THURSTON, J. N. MIDDELKAMP, and E. MASON. *Journal of Pediatrics* [*J. Pediat.*] 47, 413–423, Oct., 1955. 20 refs.

526. **Chances of Excluding Paternity by the Rh Blood Groups**
W. C. BOYD. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] 7, 229–235, Sept., 1955. 13 refs.

Anaesthetics

527. **Comparative Potencies of Thiamylal (Surital) and Thiopentone**

W. W. MUSHIN, A. G. HENDERSON, and W. W. MAPLESON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 27, 374–380, Aug., 1955. 4 figs., 8 refs.

In experiments carried out at the Welsh National School of Medicine, Cardiff, the potency of thiamylal ("surital") was compared with that of thiopentone on 16 patients undergoing serial modified electric convulsion therapy. Thiamylal, a yellow, anhydrous substance readily soluble in water to form a solution of *p*H 10 to 10·5, is the sodium salt of thioquinalbarbitone, an allyl group replacing the ethyl group of the thiopentone molecule. Its pharmacological properties resemble those of thiopentone. The effects of both drugs were observed on each patient, a dose of 25 mg. per stone (3·93 mg. per kg.) body weight being given intravenously followed by 50 mg. of suxethonium, and the shock being given when muscle twitching had ceased. During the apnoeic period inflation with oxygen was carried out by rhythmic squeezing of a rubber bag containing oxygen; after spontaneous respiration was resumed pinpricks were applied to the back of the hand until reaction to the stimulus occurred. The time of injection, the time of falling asleep (as shown by relaxation of the outstretched hand), the time of application of the shock, and the time of awakening or reaction to stimuli were noted in each case. It was found that the average duration of sleep was longer after thiamylal, but the difference was not statistically significant.

The time of recovery from a barbiturate may be influenced by the use of a relaxant, and since the same dose of suxethonium was given to all patients regardless of their weight, this influence may have been greater in some cases than in others. However, this would affect the validity of the observations only if the effect of the relaxant was different for the two barbiturates, and any such difference would be indicated statistically by correlation between body weight and the difference between the mean duration of sleep after the two drugs. No such correlation was found, nor was there any evidence that the differences in the relative size of the dose of relaxant given, by prolonging or shortening the period of muscular twitching, caused any significant variation in the time the shock was given.

The time of shock, however, appeared to affect the duration of sleep, statistical analysis of the results showing that if the shock was delayed by one second the time of awakening was delayed by an average of 5·8 seconds. The shock was given, on the average, 1·12 second later after thiamylal than after thiopentone, and correction for this factor reduces the difference between the two drugs in respect of the average duration of sleep to 18·2 seconds.

The authors conclude that their results provide no more than a suggestion that thiamylal is slightly more potent than thiopentone. Examination of a larger series of cases, however, might show that this difference was significant. *Raymond Vale*

528. **A Clinical Trial of Thiamylal as an Intravenous Anaesthetic in 1,750 Cases**

J. W. DUNDEE and J. E. RIDING. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 27, 381–387, Aug., 1955. 3 figs., 11 refs.

In this article from the University of Liverpool the authors report the use of thiamylal (thioquinalbarbitone), a rapidly acting barbiturate given intravenously, alone or in combination with other drugs for general anaesthesia in 1,750 cases drawn from the whole field of surgery. In most cases a 2½% or 5% solution was used, though in 40 cases a continuous drip infusion of a 0·4% solution was administered.

In this series thiamylal provided a rapid, effective, and pleasant induction, and appeared to be slightly more potent than thiopentone. Supplementary agents were given after thiamylal with ease, and the respiratory depression produced was equivalent to that produced by thiopentone. No case of laryngospasm or prolonged apnoea occurred. No attempt was made to assess its effect on the incidence of postoperative chest complications and vomiting. Its effect on the blood pressure was similar to that of thiopentone, and the electrocardiogram in 17 cases showed no abnormality.

To investigate the duration of thiamylal and thiopentone narcosis, 2 comparable series of patients undergoing similar operations were anaesthetized with continuous drip infusions of the two drugs in 0·4% solution and the average dose required to maintain a similar depth of anaesthesia was calculated every 5 minutes after induction. During the first 40 minutes the dose of thiopentone given was significantly larger than that of thiamylal; after one hour, however, there was no significant difference between the doses given, this being explained on the hypothesis that thiopentone has a longer action than thiamylal and therefore requires less incrementation. To compare the cumulative action of the two drugs the average supplementary doses (in mg. per kg.) required during 15-minute periods were examined, a correction factor (obtained by dividing the induction dose of thiopentone by that of thiamylal) being applied to the doses of thiamylal to allow for its greater potency. In 3 out of 4 periods the supplementary dose of thiamylal required was significantly greater than that of thiopentone. Moreover, calculation at 5-minute intervals of the ratio between the total dose given and the induction dose for the two drugs showed that the incrementation required to maintain a constant level of narcosis was significantly greater with thiamylal than thiopentone, indicating a more rapid recovery from thiamylal. *Raymond Vale*

529. **Ethyl Vinyl Ether: Pharmacological and Clinical Evaluation**

M. S. SADOVE, G. M. WYANT, and J. O. CLETCHER. *Current Researches in Anaesthesia and Analgesia* [*Curr. Res. Anesth.*] **34**, 235–240, July–Aug., 1955. 5 refs.

Ethyl vinyl ether, an asymmetrical unsaturated ether, is a volatile, colourless liquid with a not unpleasant smell; it is compatible with soda lime and all common anaesthetic agents. It does not cause any metabolic change in animals, except a 10 to 15% increase in clotting time, and is claimed to have a slightly greater margin of safety than diethyl ether.

In this paper from the University of Illinois, Chicago, the authors report the use of ethyl vinyl ether in a large series of cases (all in children) for induction of anaesthesia by the open-drop method and, more particularly, as an adjuvant to other anaesthetic agents in 29 patients aged 14 to 58 years. For induction of anaesthesia in children it is a satisfactory substitute for divinyl ether. It is a useful adjuvant to nitrous oxide–oxygen for procedures not requiring deep planes of anaesthesia. It is less irritating to the respiratory tract than diethyl or even divinyl ether, but causes the patient to cough if administration is too rapid. Conjunctival irritation occurs more frequently with ethyl vinyl ether than with either of the other ethers, and salivation tends to be severe but can be controlled by adequate doses of atropine. Ethyl vinyl ether is rapid in action, and the recovery from anaesthesia is fairly rapid. "Running movements" similar to those observed with divinyl ether may occur. Nausea and vomiting are no more frequent or severe than they are after diethyl ether. The chief change in body metabolism appears to be a temporary acetonuria. The electrocardiogram may show tachycardia or premature contractions. Irregularities in pulse, which seem to be related to the depth of anaesthesia and the total amount of drug administered, tend to disappear with lightening of the plane of anaesthesia.

Since some of the phenomena observed may well have been due to the other agents used, further studies are being carried out with ethyl vinyl ether alone to determine whether this is so. The authors consider that ethyl vinyl ether merits further clinical and pharmacological investigation. *W. Stanley Sykes*

530. **Intramuscular Suxamethonium**

I. H. MCDONALD and R. BRYCE-SMITH. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 338–345, July, 1955. 3 figs., 13 refs.

In experiments performed at the University of Oxford the authors studied the degree and duration of action of varying doses of suxamethonium chloride, given intramuscularly with and without hyaluronidase, in 157 unselected patients of all age groups, the aim of the study being to assess the value of suxamethonium as a preliminary to intubation in young children. Premedication and the type of anaesthesia varied a little from case to case, but in most papaveratrum, 1/3 grain (20 mg.), and scopolamine, 1/150 grain (0·4 mg.), were given one hour before operation, induction being with thiopentone in a standard dose of 35 mg. per stone (2·5 mg. per kg.) body weight, followed by nitrous oxide and oxygen at flow rates of 6 and 2 litres per minute respectively. Small children were premedicated with pentobarbitone, 6 mg. per kg., together with atropine sulphate, followed by ethyl chloride and open ether anaesthesia in those not fully sedated by the premedication. The cases were divided into four groups which received suxamethonium in different doses, in some cases with and in others without the addition of hyaluronidase.

From these trials the authors assessed the effect of hyaluronidase on the rapidity of onset, degree, and duration of the action of the relaxant. The addition of hyaluronidase hastened the mean time of onset of apnoea to 2 to 3 minutes, compared with 3 to 7 minutes without hyaluronidase, and the addition of this substance gave a more stable and predictable response than was found in those given the higher doses of suxamethonium alone. Fibrillary twitchings were rarely seen and could not be usefully correlated with any particular plan of administration. Blood-pressure recordings showed no abnormal variations. A peculiar finding of special interest was a prolonged period of post-anaesthetic sleep lasting up to half an hour; the authors suggest, as a possible explanation of this, some hitherto unrecognized narcotic action of the breakdown product of suxamethonium, succinyl monocholine chloride.

They are satisfied that this technique would be specially useful in infants requiring intubation, but could also be extended for general relaxation in older children and adults in whom venepuncture is difficult.

[The technique described is clearly one which merits further exploration and seems to hold out hopes of great usefulness.] *Michael Kerr*

531. **Controlled Hypotension with Arfonad in Paediatric Surgery**

S. M. ANDERSON. *British Medical Journal* [*Brit. med. J.*] **2**, 103–104, July 9, 1955. 12 refs.

In a previous paper (*Lancet*, 1951, **2**, 965) the author showed that, weight for weight, children are more tolerant of depressant and relaxant drugs than are adults. The purpose of the present paper is to show that children are also tolerant of hypotensive drugs, and that the technique of controlled hypotension can be used in operation on children with no greater danger than in adults. "Arfonad" was given by drip infusion during neurosurgical or genito-urinary operations to 44 children, 29 of whom were under 7 years of age. It was found that with a concentration of 0·1% of arfonad in the transfused fluid—the concentration generally used for adults—there was a danger of overloading the circulation if an adequate dose was given and consequently this strength was used only for children up to the age of 5 years; for children over this age the strength of the solution was doubled. The use of stronger solutions made the addition of procainamide unnecessary to secure adequate hypotension.

There was no operative death in the series, and only in 3 cases was it necessary to replace blood loss. A vasopressor drug was given in 2 cases to assist a rapid

identification of bleeding points; in all the other cases blood pressure returned to near normal within a few minutes of stopping the infusion. Hypotension and improved operating conditions were achieved in every case. *Donald V. Bateman*

532. **The Use of Hypotension in Anaesthesia for Ear, Nose and Throat Operations**
C. B. ANDREAE and H. F. GRIFFITHS. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 405–407, Aug., 1955. 2 refs.

The use of hypotension in 257 operations upon the ear, nose, and throat in hospitals of the South-East Kent Group is reported. The operations performed included submucous resection, mastoidectomy, Caldwell–Luc operation, and ethmoidectomy. It is claimed that hypotension facilitates surgery in a field where vision is often difficult, and that it obviates the need for pre- and post-operative packing of the nose, with its attendant discomforts.

Anaesthesia was induced in all cases with thiopentone, 500 mg., and gallamine triethiodide, 80 mg., followed by pethidine, 25 mg., and nitrous oxide and oxygen given through a cuffed endotracheal tube. In 182 cases hypotension was induced with hexamethonium bromide in divided doses, and in 75 cases with " arfonad " given by drip infusion of a solution containing 1 mg. per ml., all patients being operated upon in a steep reversed Trendelenburg position. Arfonad was found to provide a relatively dry field in a much larger proportion of cases than hexamethonium, and its action was much less prolonged. There were no cases of reactionary haemorrhage in this series. *Raymond Vale*

533. **Hypothermia. Part III. The Clinical Application of Hypothermic Techniques. Arteriovenous Cooling**
R. BROCK and D. N. ROSS. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **104**, 99–113, 1955. 9 figs., 21 refs.

In this report from Guy's Hospital, London, the authors describe their experience and methods of inducing hypothermia for the performance of cardiac surgery on 20 patients, mostly young. Thoracotomy is first performed at normal temperature and the diagnosis confirmed by direct observation. Hypothermia, if required, is then induced by withdrawing the blood through a catheter in the superior vena cava, pumping it through a cooling coil by means of a hand-driven rotary pump, and returning it to the inferior vena cava, both venae cavae being entered through the right atrial appendage. By this method the rate of cooling is readily controlled, cardiac irregularities can be dealt with at once since the chest is open, and the period of hypothermia is minimized, as rewarming can be begun while the chest is being closed. To secure a dry heart for repair of septal defects the venae cavae, pulmonary veins, aorta, and pulmonary artery are clamped, but in order to maintain adequate coronary circulation the left pulmonary vein is left unclamped. The patient's temperature is recorded by mercury thermometers in the pharynx and chest, under the control respectively of the anaesthetist and surgeon.

The complications are discussed. Ventricular fibrillation is treated by cessation of the cooling, cardiac massage, and electrical defibrillation, but during cardiotomy these measures are not instituted until repair of the defect is completed. In addition the intracardiac injection of adrenaline (5 to 10 ml. of 1:10,000 solution in saline) or warm saline applied to the myocardial surface may be used. Between temperatures of 36° and 28° C. the most important factor preventing ventricular fibrillation is adequate coronary flow, and neostigmine helps by slowing the heart. Air embolism can be avoided by keeping the septal defect uppermost, by not passing the sucking cannula down through it, and by flooding the heart with normal saline before closing. Coronary air embolism is treated by pricking minor coronary side-branches and milking out the air bubbles, and this, if followed by cardiac massage, is generally effective. Various methods of rewarming are discussed. Venous rewarming, begun immediately the cardiotomy is closed, has been tried by inserting fresh catheters into the venae cavae and pumping the blood through the original coil, now immersed in warm water at 40° C., until the body temperature reaches 32° C.; this takes about 20 to 30 minutes and can be carried out while the chest is being closed. Rewarming by means of a " radio-frequency " coil, surface warming by a rubber blanket, and rectal warming have also been used. *B. L. Finer*

534. **Electrocardiographic Findings during Laryngoscopy and Endotracheal Intubation**
J. A. G. HORTON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **27**, 326–337, July, 1955. 12 figs., 12 refs.

Continuous electrocardiograms (ECG) were recorded at the Royal Victoria Infirmary, Newcastle upon Tyne, from 219 patients during laryngoscopy or endotracheal intubation under light or deep general anaesthesia. Bradycardia during intubation was observed in some patients given thiopentone and relaxant drugs, and although bradycardia did not occur when intubation was performed under deep anaesthesia—thus possibly supporting the view that this method gives greater safety—changes in the ECG (depression of the S–T segment, inversion of waves P and T, or A–V nodal rhythm) were quite common and might be considered indicative of vagal overtone or myocardial hypoxia. There was sinus tachycardia (over 100 beats per minute) in only 17 cases as a sequel to intubation, while in 60 cases sinus tachycardia was present before intubation, the rate being slowed after the procedure in 13 of these.

Laryngoscopy and unsuccessful attempts at intubation were followed by bradycardia more commonly than was actual intubation. Attempted intubation was sometimes accompanied by changes in the ECG typical of hypoxia. Evidence of cardiac irritation was the appearance of ventricular ectopic beats, but no case of ventricular tachycardia occurred. Ectopic beats were more common in patients deeply anaesthetized, in those given the halogen drugs, and in older patients. In the whole series, however, none of the changes seen was severe and evidence of cardiac inhibition was minimal.
T. Semple

Radiology

EXPERIMENTAL

535. **The Influence of Strychnine on the Biological Effect of Ionizing Radiation.** (О влиянии стрихнина на биологическое действие ионизирующего излучения)
G. TENCHOV, S. BALUEV, and A. SAKHATCHIEV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 14–21, No. 4, July–Aug., 1955. 6 figs., 18 refs.

A study of the influence of strychnine on the biological effects of ionizing radiation was carried out on white rats which were subjected to whole-body irradiation from an *x*-ray apparatus with the following technical factors: 180 kV, 10 mA, 3 mm. Al filter with H.V.L. equal to 0·75 mm. Cu. The dose of *x*-radiation was 800 r for some batches of rats and 930 r for others. Two groups of animals received a dose of 0·0625 mg. of strychnine subcutaneously immediately after the irradiation, a third batch (which received 800 r) were given the same dose of strychnine before the irradiation, while a fourth (control) group received no strychnine.

All the animals which received strychnine after the irradiation lived longer and lost less weight than the animals which received no strychnine, whereas those rats given strychnine before the irradiation showed increased sensitivity to irradiation. These laboratory findings in rats were confirmed clinically in human subjects, in that patients suffering from malignant disease who received strychnine after *x*-irradiation did not develop irradiation sickness.

The authors discuss the mechanism of action of strychnine on the tissues of the body and conclude that strychnine exercises its effect through the nervous sytem.

A. Orley

536. **The Destructive Effects of Radioactive Iodine**
J. A. FORBES. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 378–380, July, 1955. 2 figs., 5 refs.

In a study carried out at the University of Melbourne the destructive effects of radioactive iodine (^{131}I) were examined in rats inoculated with thyroid carcinoma transplants. Doses of 3 mc. were given to ablate the normal gland, and the tumour tissue was then attacked by doses of 1 to 3 mc., which were sometimes repeated. Autoradiographs of sections showed very patchy distribution of the ^{131}I in the neoplastic tissue, but more uniform distribution in the normal gland. Thus single large doses may destroy a normal thyroid gland but only patches of a tumour. Examination 12 weeks after a dose showed the gland to be completely replaced by fragments of yellow tissue, and if left longer this might become completely calcified. Microscopically, the yellow tissue consisted of fairly avascular collagen and scattered fibroblasts. At an intermediate stage remnants of active gland tissue were seen, with radionecrotic debris. There was a striking absence of early inflammatory changes, probably due to coagulative and thrombotic effects of the radiation.

In tumour tissue there was no uptake of ^{131}I in the uniformly cellular growths without vesicles or in the cellular areas of well-differentiated tumours. In the latter type of tumour, therefore, destructive effects were very patchy and treatment in such cases can only be palliative; in the well-differentiated area radionecrotic changes and fibrosis resembled those in the normal gland. Changes were demonstrated in metastases in the trachea, which, it is suggested, may be one route of expulsion of necrotic debris. Treatment with ^{131}I can reduce the amount of secretion in tumours and delay their enlargement, and also obstruction of bronchi or pressure on the spinal cord by metastases can be hindered. In secondary growths in the lung a possible hazard is cavitation with infection and collapse. A single dose of ^{131}I may suffice to ablate a normal gland, but repeated doses are essential to obtain the maximum destructive effect on tumours. Regeneration of tumour cells was noted around blood vessels, this finding emphasizing the temporary nature of the arrest of growth. The absence of inflammatory changes obviates the danger of respiratory obstruction and suggests that subsequent surgery may be made easier.

J. Walter

537. **Use of Radioactive Potassium (K^{42}) in the Study of Benign and Malignant Breast Tumors**
W. H. BAKER, I. T. NATHANSON, and B. SELVERSTONE. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 612–615, April 14, 1955. 2 figs., 5 refs.

Radioactive potassium (^{42}K) has been shown to be localized in high concentration in tumours of the brain, the high intensity of its gamma-ray emission enabling the presence of such a tumour to be detected with a counter placed on the surface of the head. To determine its potential value in the detection of malignant tumours of the breast, ^{42}K in the form of irradiated potassium carbonate was injected intravenously at the Massachusetts General Hospital (Harvard Medical School), Boston, into 102 patients with a tumour in one breast.

Using a counter with a cylindrical lead shield to collimate the gamma-ray beam, the authors observed a significant (20%) increase in the counting rate on the affected side compared with that over the normal breast in 80% of the cases of malignant tumour, all of which were verified histologically. The difference in uptake was greatest 5 to 15 minutes after injection. In none of the cases of benign tumour was there so great a differential uptake, the increase in counting rate being always less than 20%, and less than 10% in the 4 cases of inflammatory tumour tested. Since the increase in counting rate in 13 of the cases of malignant tumour was

within the same range, however, it is concluded that failure to show a significant difference between the counting rate over the tumour and that over normal breast tissue after the injection of ^{42}K is not conclusive evidence of its benign nature, although a difference of 20% or more appears to offer presumptive evidence that the mass is malignant.

[It is stated that 102 cases were studied, in 38 of which the tumour was benign. The number of cases of malignant tumour studied, however, is variously given as 65 or 66, making the total either 103 or 104.]

Jan G. de Winter

538. **The Late Effects of Thorotrast Administration. A Review and an Experimental Study**

J. P. GUIMARAES, L. F. LAMERTON, and W. R. CHRISTENSEN. *British Journal of Cancer* [*Brit. J. Cancer*] **9**, 253–267, June, 1955. 22 figs., 33 refs.

In the first part of this paper from the Royal Marsden Hospital, London, the literature on the late effects of thorotrast, with particular reference to its carcinogenic effects in man and animals, is critically reviewed. In the second part an investigation is reported of the effect in the mouse of intravenous injection of thorotrast, with and without the addition of whole body *x*-irradiation. The number of animals studied was small, but the survival times of control and treated mice did not indicate that the injection of thorotrast increased mortality within a period of 15 months. The necropsy findings in 12 animals dying 13 to 21 months after the injection are described. All the animals showed degenerative changes in the liver; in addition 5 had hepatomata, one had a reticulo-endothelioma of the liver, one a haemangio-endothelioma of the spleen, and 7 had lung tumours. Macroscopical examination of control animals surviving over 12 months did not reveal any evidence of a tumour.

L. A. Elson

RADIODIAGNOSIS

539. **Radiographic Use of Lead E.D.T.A. in Man**

N. SAPEIKA. *British Medical Journal* [*Brit. med. J.*] **2**, 167–169, July 16, 1955. 3 figs., 7 refs.

The use of lead disodium EDTA complex as a radio-opaque medium in the human subject is described in this paper from the University of Capetown. In one investigation the lead complex was incorporated in a thick mucilage of starch (20%) in a concentration of 1 g. in each gramme of mucilage, and 5 g. was swallowed on 5 occasions by 3 healthy adults. No gastric or other intestinal disturbance was observed, but the stools were black and remained so for a few days. Radiographs of the oesophagus showed satisfactory density of the contrast medium.

In another investigation the lead complex was administered intravenously in 50% concentration in sterile aqueous solution to 4 patients and radiographs were taken of the urinary system. In 3 cases 18 ml., 15 ml., and 9 ml. of the solution respectively was injected, and apart from temporary discomfort at the site of injection there was no evidence of any reaction. In the remaining case 27 ml. was injected and the patient complained of abdominal discomfort about 20 minutes later; some hours after the injection the temperature rose and dark urine was passed. Examination of the blood and urine indicated an intravascular haemolysis from which, however, there was apparently complete recovery.

Lead EDTA in sterile 0·9% sodium chloride solution was also used for radiological examination of the nasal sinuses, the concentrations employed being 5%, 7·5%, 17·5%, and 20%. Shadows of good density were obtained and no untoward effects were noted.

[No comparison is made between the density of the shadows with this medium and that obtained with other substances similarly used.] *L. G. Blair*

540. **Phlebographic Study of Tumours of the Cerebral Hemispheres.** (Étude phlébographique des tumeurs hémisphériques)

—. LAINE, —. DELANDTSHEER, —. GALIBERT, and —. DELANDTSHEER. *Neuro-chirurgie* [*Neuro-chirurgie*] **1**, 5–28, 1955. 20 figs., 6 refs.

In carrying out cerebral arteriography for the diagnosis of tumour the authors use a "carrousel" accommodating 6 cassettes which are exposed during the injection of contrast medium at intervals of 0·75 second. Six such exposures are made for each antero-posterior and lateral position. The authors have worked out a normal "topogram" of the foramen of Monro consisting of an arrow and a small triangle drawn on a transparency. This transparency is superimposed on the given phlebogram and any deviation of the deep veins from the normal is ascertained by measurement. It is therefore essential that all angiograms be obtained by means of a standard technique using the same incidence of the central ray and the same focus–skin distance. They claim that the superimposition of the topogram transparency reveals at a glance the majority of parietal, frontal, and fronto-polar tumours. The appearance of the striothalamic vein is of capital importance and allows an appreciation of the degree of malignity of the tumour.

[The main value of this paper lies in the numerous excellent diagrams and radiographic illustrations, which should be consulted in the original by those interested in the subject.] *A. Orley*

541. **Cervical Air Myelography. A Review of 130 Cases**

F. MURTAGH, W. E. CHAMBERLAIN, M. SCOTT, and H. T. WYCIS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **74**, 1–21, July, 1955. 13 figs., 23 refs.

In this paper from Temple University Medical School and Hospital, Philadelphia, the authors present a survey of 142 individual myelographic studies of the cervical region made on 130 patients with air as the contrast medium. The technique is described in full detail.

In the first 24 cases small quantities of air (5 to 10 ml.) were used, and in 17 of these the lower level of a complete or nearly complete block was successfully demonstrated. In the 7 remaining cases the air passed into the cranial

cavity and although the absence of a block was demonstrated, no other information was obtained concerning the condition of the cervical spinal canal. It was therefore felt that a more adequate method of visualizing the cervical canal was needed, and a procedure was devised whereby 40 to 50 ml. of air placed in the lumbocaudal canal is manœuvred into the cervical region. Of 59 studies made in this manner, in 47 satisfactory visualization of the cervical canal was obtained. In a further 59 cases the cerebrospinal fluid was drained completely from the subarachnoid space and replaced by air. The authors state that this method is particularly valuable for the visualization of non-obstructive lesions such as disk protrusions and spondylosis. Satisfactory visualization of the cervical cord was obtained, together with air encephalograms, in 48 cases. The antero-posterior projection is of little use owing to the superimposed tracheal air shadow, and the authors find that the lateral projection in both prone and supine positions after total drainage of the cerebrospinal space and air replacement are the most valuable. Myelography with " pantopaque " (ethyl iodophenylundecylate) was used in a number of cases after inconclusive results with air myelography, but did not add any useful information.

The authors state that air and other gaseous media are the only innocuous and completely absorbable contrast media available for myelography. They do not put forward air myelography as a substitute for myelography with opaque media, but consider that it has a definite value as an effective and harmless method of surveying the suspected portion of the spinal canal which may often give sufficiently accurate information and in some cases may even demonstrate lesions which cannot be seen with positive contrast.

[This is an interesting plea for the reinstatement of air myelography, but the abstracter would agree with the authors' statement that even with the excellent contrast obtainable by modern radiographic techniques the interpretation of the films is difficult and the possibility of error much greater than with opaque media. There is a great need for an innocuous and readily absorbed contrast medium for spinal myelography, but air cannot supply this need, even when the careful technique described in this paper is used.] *J. MacD. Holmes*

542. **The Ageing Vertebral Column (Macro- and Historadiographical Study)**

F. Bohatirchuk. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 389–404, Aug., 1955. 19 figs., bibliography.

Scant attention has been paid in the past to the normal physiological changes associated with the ageing of bone in the spine, although it was suggested by Junghanns in 1931 that both atrophic and hypertrophic changes may occur as a part of the normal ageing process. The possibility of a physiological osteoporosis has since then been widely accepted. On the other hand although the term " spondylosis " may be used to avoid the suggestion of an inflammatory process, nevertheless many authors regard hypertrophic changes as being due always to a pathological process. In the past 20 years, however, many observations have been reported which suggest that with advancing years hypertrophic and atrophic changes develop in the skeleton which are not the result of disease, the radiological appearances being typical for each age group. The author, working at the University of Ottawa, has therefore studied the changes in radiographs of the spine of 75 apparently healthy persons aged 40 to 94 (50 males, 25 females) in order to determine the characteristics differentiating normal from pathological ageing changes, and has compared them with changes in the spine of ageing animals. In addition, some 600 historadiographs of human and canine bone at various ages were examined. These were made by the indirect method using a fine-grain emulsion, magnification up to $\times 300$ being obtained.

Evidence of bone atrophy was found in the spine from the age of 50 to 55 years onwards. It is stressed that although the atrophy progresses with age, the vertebrae retain their shape even when vertical trabeculae alone are to be seen. Extreme porosis with compression fractures, cavities in the spongiosa, and destruction of the peripheral compact bone indicate a pathological process. It is estimated that lipping of the vertebral bodies is found in 60 to 80% of the population over the age of 40 years. Under the age of 60 years the lipping tends to be symmetrical, but in later life it is generally asymmetrical. Fusion of neighbouring areas of lipping may occur. Pronounced local asymmetry of lipping is a feature of cases of scoliosis and those with a history of trauma. The degree of limitation of movement present could not be correlated with the degree of hypertrophic change. Very extensive lipping, with fusion, and severe rigidity of the spine, together with the formation of loose bodies and extensive calcification or ossification of the anterior longitudinal ligament, are features suggesting a pathological process rather than normal ageing. However, the author stresses that in making such a differentiation it is of the greatest importance to consider the adaptation of the individual to the ageing process, and that apparently pathological changes are to be found in clinically healthy old people. The ageing changes found in the spine in dogs were very similar to those in the human subjects.

The historadiographic findings are discussed, and it is suggested that further consideration must be given to the theory of halisteresis as a mechanism of bone absorption.

Kenneth A. Rowley

543. **The Value of Frontal Oblique Tomography in Determining the Extent of Involvement in Bronchial Cancer.** (Intérêt de la tomographie frontale-oblique dans l'appréciation de l'extension des cancers bronchiques)

J. C. Rudler, C. Frain, J. Roujeau, and P. Bordessoule. *Poumon et le Cœur* [*Poumon et Cœur*] **11**, 477–486, June–July, 1955. 9 figs.

In coming to a decision on the best treatment of a bronchial carcinoma an exact knowledge of its local extension is a fundamental requirement. It is the authors' view that in spite of advances in the interpretation of radiographs and bronchoscopic appearances, too many exploratory thoracotomies are still carried out, and they suggest that equally valuable information can

be obtained by frontal oblique tomography. They recommend that tomographic exploration of those portions of the tracheobronchial tree visible in the frontal plane should be carried out, using very thin cuts orientated in the chosen plane, for which a big angle of swing and the possibility of positioning the film from the horizontal to the vertical are necessary. For these reasons they have had constructed a tomograph which fulfils these requirements and with which, by the addition of a movable cassette holder, frontal oblique exposures can be made. They state that cuts of 1 mm. in thickness allow the precise location of lesions anterior or posterior to the tracheobronchial tree.

In reviewing the results all tomograms must be examined, since an appearance of stenosis may be given if the trachea or bronchus passes out of the plane of the cut. Suspicious opacities should be examined in several cuts. Normally the whole of the tracheobronchial tree can be seen, together with the great vessels related to it, and when a tumour is present it gives the appearance of stenosing or amputating the arterial branches. It may occasionally be difficult to distinguish a tumour from the pulmonary artery, but a tumour always has a greater opacity than the artery and may cause deformity of the carina, or in some cases extension to the opposite side may be seen. The authors agree that frontal oblique tomography is not a substitute for bronchoscopy in diagnosing malignancy, but point out that it does show very much more. A number of illustrative case histories with reproductions of tomograms are presented.

John H. L. Conway-Hughes

544. **Preliminary Clinical Evaluation of Hypaque in Excretory Urography**

R. M. Lowman, H. Shapiro, A. Lin, L. Davis, F. E. Korn, and H. R. Newman. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **101**, 1–8, July, 1955. 3 figs., 8 refs.

"Hypaque" (sodium 3:5-diacetamido-2:4:6-triiodobenzoate), a new contrast medium for intravenous urography, has been used in 300 cases at the Grace–New Haven Community Hospital–Yale Medical Center. In this paper the results obtained in these cases are compared with those previously obtained with diodone. An injection of 20 to 30 ml. of a 50% solution of hypaque was given in 2 to 3 minutes, and the resulting urograms were regarded as being "good" or "excellent" in quality in 85% of cases. The medium was found to resemble "urokon" ["diaginol"] in that it was excreted more rapidly than diodone, so that the kidneys were visualized earlier, and that the delineation of the pelvis and calyceal system was sharper.

Preliminary sensitivity tests were carried out in all cases, but were considered to be unreliable. Reactions occurred in 8 patients in whom no evidence of sensitivity had been found on testing, and included nausea, vomiting, flushing of the face, and dizziness, but there were no "true allergic" reactions such as sneezing, coughing, dyspnoea, or urticaria. Four patients experienced tingling or burning of the lips, mouth, or extremities, and in 1 out of 15 cases in which the urine was examined there was transient albuminuria. There were no serious local reactions, and injection of "a moderate amount" of the medium into the soft tissues in one case caused only temporary aching. In 80 cases the blood pressure was measured before and after the injection; in 65% of these there was an average fall of 8 mm. Hg in systolic and of 4 mm. Hg in diastolic blood pressure. No correlation was found between blood-pressure fluctuations and toxic reactions.

[The main clinical value of this paper lies in the relatively small number of toxic reactions reported. The other clinical data are too scanty for adequate appraisal, whereas a considerable amount of space is devoted to an account of animal experiments, apparently carried out by the manufacturers, of which the details have not been published, and to a rather speculative discussion of the possible mode of excretion of the medium.]

G. Ansell

See also The Rheumatic Diseases, Abstract 452.

RADIOTHERAPY

545. **Neoplasia in Children Treated with *X*-rays in Infancy for Thymic Enlargement**

C. L. Simpson, L. H. Hempelmann, and L. M. Fuller. *Radiology* [*Radiology*] **64**, 840–845, June, 1955. 16 refs.

Because of the possibility that late sequelae may develop some time after *x*-ray therapy, a follow-up survey of 1,722 children treated by this means for enlargement of the thymus gland between 1926 and 1951 was carried out, the cases being obtained from the records of three hospitals and three private practices in the States of New York and Washington. The children treated at one of the hospitals usually had respiratory symptoms at the time of treatment; in the other cases treatment was given because of radiological evidence of thymus enlargement. Most of the children in the latter group were less than 2 weeks old at the time of treatment, whereas those in the former group were several weeks old, but all were under one year of age. Doses (in air) varied from 50 to 1,500 r, the great majority of patients receiving less than 600 r.

Information concerning the present state of health of 1,400 of the 1,722 treated children and of 1,795 of their untreated siblings was obtained. Of the treated children, 67 had died, compared with 56 of the untreated siblings. Cancer had developed in 17 of the treated children (9 of whom were dead), while 4 of the untreated siblings had died of cancer and one had had a growth removed. In addition, 6 children in the treated group had a thyroid adenoma and 2 had thyroid nodules compared with one case of thyroid adenoma among the siblings. In the treated group there were 7 cases of leukaemia and 6 of carcinoma of the thyroid, whereas there was no case of these conditions among the untreated. The development of leukaemia was not associated with high dosage, but all the cases of other forms of neoplasia in treated children occurred in the group known to have received more than 200 r.

I. G. Williams

546. **Malignant Epibulbar Melanoma.** (Das maligne epibulbäre Melanom)
G. NOTTER. *Strahlentherapie* [*Strahlentherapie*] **96**, 517–537, April, 1955. 15 figs., bibliography.

The author reviews 35 cases of epibulbar melanoma treated at Radiumhemmet, Stockholm, between 1921 and 1953 by surgery, radiotherapy, or a combination of the two. He concludes from this analysis that radiotherapy should be the first choice of method for all flat lesions, thick lesions which would otherwise necessitate enucleation of the eye, for lesions that have been incompletely excised or have recurred, and in those cases in which operation is refused.

As standard treatment he recommends 5 to 10 doses each of 2,000 βr given over 4 to 9 days by means of a radioactive strontium (^{90}Sr) applicator. Biopsy should be performed after the first three doses.

Of the 35 patients treated, 14 remain symptom-free, 3 of these having been treated solely by radiation. A further 14 patients died from metastases and 6 from intercurrent disease. The 5-year cure rate was 43% and the 10-year cure rate 28%. *Jan G. de Winter*

547. **Cancer of the Middle Ear and External Auditory Meatus**
J. BOLAND and R. PATERSON. *Journal of Laryngology and Otology* [*J. Laryng.*] **69**, 468–478, July, 1955. 2 figs.

In this paper a total of 143 cases of carcinoma of the middle ear and external auditory meatus seen at the Christie Hospital, Manchester, since 1932, are reviewed. In this hospital in the last 2 years radical treatment by multiple teleradium fields has been given in such cases; earlier, single- and multiple-field deep *x*-ray therapy, intracavitary radium, or a combination of these was employed.

In 26 cases the disease was confined to the external meatus, but 6 of these were excluded from the series because histological evidence of carcinoma was not available. In 4 of the 20 histologically proven cases there were metastases to the cervical lymph nodes. The average age of the 20 patients (7 females and 13 males) was 62 years. Radical treatment was given to 11 of these patients, 9 of whom survived 5 years or more.

The middle ear or mastoid cells were involved in 117 cases; 31 of these were excluded from the series (6 with basal-cell tumour, 8 with glomus tumour, and 17 in which there was no histological proof of malignancy). Of the remaining 86 patients (42 males and 44 females), 49 admitted long-standing aural discharge; the authors state that in the majority of patients in this group the undoubted remote cause of carcinoma was chronic suppuration. The history was typical; in most cases there was pain or facial palsy many years after an infection of the ear, usually in childhood. The submento-vertical radiograph was found to be most valuable in assessing the extent of bony destruction. Metastases to cervical lymph nodes were present when the patient was first seen in 10 cases and developed in others subsequently. Post mortem, metastases were found in the lung in one case, in the skeleton in one, and in the liver in 2 cases.

Intracavitary radium in these cases was abandoned in 1938 for 250-kV or 500-kV *x* rays by multiple small fields, usually one on the affected side and 4 to 6 on the contralateral side. The patient wore a jig helmet, and the high dose volume included the whole of the petrous temporal bone. None of the 7 patients given 5,500 r in 3 weeks survived, the reaction to the dose being severe and prolonged; of 20 patients given 5,000 r in 3 weeks, 6 survived 5 years.

The authors state that from experience in these cases they do not consider surgical intervention before radiotherapy to be advisable. Bone necrosis was not troublesome, but irradiation damage to the brain stem was the most lethal complication, there being proven or suspected damage in 6 out of 27 patients receiving radical *x*-ray therapy. *G. E. Flatman*

548. **Observations on the Use of Chlorpromazine Hydrochloride in Radiation Sickness**
D. O'CONNELL. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **6**, 214–216, Jan., 1955. 11 refs.

The chemical structure and pharmacology of chlorpromazine (" largactil ") are discussed. The drug has a marked anti-emetic action, especially when vomiting is centrally induced, and in view of this it is advocated for the control of radiation sickness. In general, nausea and vomiting from radiation sickness are reduced, in some cases being completely allayed, but diarrhoea is unaffected.

Out of 38 patients at Charing Cross Hospital, London, who were given 25 mg. of chlorpromazine three times a day, 20 were completely relieved of symptoms of radiation sickness and 15 were sufficiently relieved to continue radiotherapy. Drowsiness was the commonest side-effect, and 3 patients suffered from depression and headache. Subacute toxic hepatitis developed in 2 cases, and the cause of this is discussed.
R. D. S. Rhys-Lewis

549. **Radiation Sickness in Man following the Administration of Therapeutic Radioiodine. Relationship between Latent Period, Dose-rate and Body Size**
J. D. ABBATT, W. M. COURT BROWN, and H. E. A. FARRAN. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 358–363, July, 1955. 5 figs., 11 refs.

Following the administration, orally in all but 5 cases, at the Postgraduate Medical School of London, of 44 doses of radioactive iodine (^{131}I) ranging from 29 to 200 mc. to 38 patients suffering from various conditions (cardiac disease with or without thyrotoxicosis, and carcinoma of the thyroid in various stages), radiation sickness was observed in 28 cases. The syndrome showed two phases, the first appearing within 24 hours and the second in 5 to 9 days. In the first phase the symptoms resembled those seen after medium-voltage *x* rays, with a latent interval of 4 to 13 hours (mean 8 hours) and consisted in fatigue, headache, nausea, and sometimes vomiting; these passed off in 24 to 36 hours. The second phase was seen in only 11 of the cases. It was always preceded by the first phase and resembled it, except that the symptoms were usually less severe; it was

associated with local symptoms of " radiation thyroiditis ", with tenderness in the thyroid gland on swallowing or palpation which might last 2 to 3 weeks. (Similar symptoms may also occur in localized secondary deposits.)

The mode of production of radiation sickness is unknown, but it is thought to depend on the formation of a diffusible metabolite which reaches a critical threshold of concentration in some compartment or compartments of the body. The development of sickness depends to some extent on body size; if body-fluid compartments are distorted by cardiac disease, the relationship between body size and the onset of symptoms is also distorted. In this series no correlation was found between the radiation dose to thyroid tissue and incidence of symptoms or length of the latent period; but the severity of symptoms is due to the irradiation of nearly the whole body which occurs, and can be attributed to radioactivity in the extracellular fluid in the first few hours after absorption, before this is reduced by thyroid and renal clearance. There was no correlation between the total dose of ^{131}I and the duration of the latent period, but there was a highly significant relationship between dose rate per unit of body size and latent period. This suggests that the dose rate is an important factor in determining the incidence and time of onset of radiation sickness. *J. Walter*

550. Radioactive Colloidal Gold: a Simple and Safe Technique for its Administration

N. SIMON and J. MELAMED. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **22**, 91–95, July–Aug., 1955. 3 figs., 7 refs.

In the past 3 years at the Mount Sinai Hospital, New York, the authors have treated with radioactive gold (^{198}Au) 100 patients with effusions due to malignant disease. From this experience they have evolved a simple and safe technique, using expendable plastic material, whereby no member of the team administering the gold received more than 3 milliroentgens of whole-body irradiation in a single treatment. A complete and detailed description, with diagrams, of the method and apparatus used is given [and should be consulted in the original]. The method can be adapted for the administration of ^{198}Au either intrapleurally or intraperitoneally. [This would appear to be a satisfactory method of introducing radioactive gold by remote control and of limiting the possible exposure to irradiation of the operator.] *M. P. Cole*

551. Radioactive Gold Treatment: Results in 85 Effusions Due to Cancer

N. SIMON. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **22**, 96–98, July–Aug., 1955. 1 ref.

The author has used radioactive gold (^{198}Au) in the treatment of 85 patients with effusions due to carcinoma at the Mount Sinai Hospital, New York, since July, 1951. The treatment was regarded as having had a beneficial effect if the frequency of aspiration was reduced. At first patients were selected for treatment only if multiple aspirations had been required, but more recently patients have been treated at the time of the first aspiration, the result of treatment in such cases being described as " uncertain ".

Of 46 cases of pleural effusion a favourable result was obtained in 20 (43%). The commonest cause of effusion in these cases was carcinoma of the breast; 20 cases of this disease were treated, with a favourable result in 13 (65%); on the other hand, only in 2 out of 8 cases of carcinoma of lung was a favourable result obtained. The author considers that it is reasonable to expect a better response in cases of effusion due to carcinoma of the breast than in cases of carcinoma of the lung, as the latter is often a rapidly progressive disease compared with the former.

Of 39 patients with ascites secondary to carcinoma, 13 (33%) showed a favourable response to treatment; 22 of these patients had carcinoma of the ovary, of whom 7 (31%) responded favourably.

The author concludes that although better statistical results could be obtained by selecting for treatment only those patients with the slower growing carcinomata of the breast and ovary, the occasional good results obtained in cases of effusions due to other primary tumours justify the use of this method in a wider range of cases. *M. P. Cole*

552. Follow-up Study of One Hundred Cases of Carcinoma of the Prostate Treated with Radioactive Gold

H. D. KERR, R. H. FLOCKS, H. B. ELKINS, D. CULP, and T. C. EVANS. *Radiology* [*Radiology*] **64**, 637–641, May, 1955. 1 fig., 2 refs.

Colloidal radioactive gold (^{198}Au) was used at the State University of Iowa, Iowa City, in the treatment of 152 cases of carcinoma of the prostate, 100 of these being followed up for at least 2 years and 52 for at least one year. In all cases histological confirmation of the diagnosis was obtained by retropubic exploration and biopsy. The condition was inoperable, but no distant metastases could be demonstrated. In earlier cases ^{198}Au was injected into the malignant mass at operation, supplementary injections being given later, if necessary, into any recurrent nodules through the perineum. It was hoped in this way to destroy the whole mass, but the authors later realized that only very small tumours could be sterilized by injection of ^{198}Au alone. In the present series as much tumour tissue as possible was excised, including any lymph nodes involved, and ^{198}Au was injected into the remaining tumour tissue, the dosages employed being 80 to 125 mc. in about 10 to 12 ml. of fluid, with a safe maximum of 175 mc.; a ratio of about 2 mc. per gramme of tissue was the aim. Multiple small injections were given under high pressure. Of the first 50 patients, 7 developed rectal ulceration, 4 requiring colostomy; this complication was not encountered subsequently and the authors state that it can be avoided by careful distribution of the gold. Calculi may form in a necrotic mass but they are small and can be removed with a resectoscope, or crushed and washed out.

Of the first 100 patients, 48 were alive after 2 years, 28 of them without evidence of carcinoma. *E. Stanley Lee*

History of Medicine

553. **An Unrecognised Medical Periodical—*Collectanea Hibernica Medica***
J. D. H. WIDDESS. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 377–379, Aug., 1955. 1 fig.

In 1762 an Irishman named Richard Harris took the degree of M.D. at Edinburgh with a thesis entitled *De abortu*; thereafter he practised in Clonmel, where he appears to have specialized in obstetrics. In 1783 he published a work of 113 pages with the ambitious title *Collectanea Hibernica Medica*, which was printed in Dublin, containing four papers on medical subjects written by himself. That he meant this to be the first of a series is clear from the title page, which states: "Number 1. Written entirely as an Experiment of Public Taste, as well as to make a Beginning." Regular publication was not intended, for the editor expressly states that the purpose was "to register, and hand to posterity, the experiments, the opinions of men, without the trouble and inconvenience of a professed publication". No second number has been traced and it must therefore be concluded that the project was stillborn.

Zachary Cope

554. **The Birth of Vopiscus Fortunatus Plempius.** (La naissance de Vopiscus Fortunatus Plempius)
L. GLESINGER. *Scalpel* [*Scalpel* (*Brux.*)] **108**, 673–678, June 25, 1955. 1 fig., 20 refs.

The author discusses the possible reasons why Plempius (1601–71), professor in the Louvain Faculty of Medicine, possessed the unusual names of Vopiscus Fortunatus. According to Abraham Titsingh (1684–1776), a Dutch obstetrician quoted by Sprengel (1827), the name Fortunatus was given to him as a result of his survival following birth by Caesarean section after the death of his mother. Although the name Fortunatus was undoubtedly an allusion to some extraordinary circumstance attending the child's birth, Titsingh's explanation is unlikely in the extreme. Such operations were occasionally performed during the 17th century, but the infant hardly ever survived the interval which, to make quite certain of the mother's death, was generally allowed to elapse before the operation was carried out. Moreover, Titsingh described the circumstances of Plempius's birth some 150 years after the event, so that the accuracy of his information is necessarily suspect.

Vopiscus, not being a Christian name recognized by the Church, could not have been given to Plempius at his baptism, and it seems certain that he did not assume the name until 1632. It is probable that he was persuaded to do so by his reading of Pliny's *Natural History*, in which the term *vopiscus* is applied to the survivor of a twin pregnancy in which one foetus, having died early in pregnancy, has been cast out as an abortion. Such an occurrence is extremely rare, and perhaps the more likely explanation is that Plempius's twin was either stillborn or died shortly after birth, a circumstance which might also account for the survivor's second name. But after 350 years it is impossible to determine the exact truth.

H. P. Tait

555. **Neisser and Neisserian Principles in Venereology**
L. W. HARRISON. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **31**, 65–73, June, 1955. 39 refs.

The author of these biographical notes on Albert Neisser, the centenary of whose birth fell on January 22, 1955, stresses especially the fact that Neisser, besides having discovered the gonococcus, has rendered great service to modern venereology by putting the treatment of gonorrhoea on a rational basis. He not only protested successfully against the use of strong astringents, but insisted that treatment should be controlled by repeated microscopical examination of the discharge. Neisser also proved to be the originator of what is nowadays called the synergistic treatment of syphilis when he introduced the use of arsenic and mercury in combination. He played an important part at the conferences in Brussels in 1889 and 1902 when the international campaign against venereal disease was inaugurated, and in the latter year was one of the founders of the German Society for Combating Venereal Disease. The present author recollects how from 1912 onwards he himself introduced Neisserian principles into the treatment of gonorrhoea in Great Britain. He is convinced that these methods, once they were generally adopted, led to a remarkable decline in the incidence of post-gonorrhoeal stricture of the urethra. He also expresses the opinion that the treatment of early syphilis with concurrent injections of an arsenic compound and an insoluble mercury compound has prevented a great number of cases of meningovascular neurosyphilis.

A. Fessler

556. **Paul Ehrlich and His Impact on Dermatosyphilology**
H. PINKUS. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **72**, 113–119, Aug., 1955. 1 fig., 19 refs.

557. **William Harvey and Italy.** (William Harvey et l'Italie)
L. CHAUVOIS. *Archivio italiano di scienze mediche tropicali e di parassitologia* [*Arch. ital. Sci. med. trop.*] **36**, 383–400, July, 1955. 6 figs., bibliography.

William Harvey was 19 years of age when, in 1598, he left Cambridge as Bachelor of Arts and went to Padua to take up his medical studies. His choice of university was governed not only by the renown which Padua had recently gained through great teachers like Fallopius, Vesalius, and Realdo Colombo, but also by the presence of their pupil Fabricius, himself already famous. It was also no doubt influenced by the more liberal spirit there prevailing under the rule of the Republic of Venice,

which made it more congenial to students from Protestant countries, particularly England. But even here there was frequent strife between the students of the University and the Jesuit colleges: between the spirit of progress and religious fanaticism.

It was in this atmosphere that Harvey began to have his doubts about the Galenic dogma regarding the circulation of blood. He was not the first to think in this way. Michael Servetus, in his *Christianismi restitutio*, postulated the presence of the pulmonary circulation, for which belief and other views he paid with a martyr's death at Geneva in 1553. Moreover Andrea Cesalpino of Rome (1519–1603), in his *Quaestionum medicarum* Libri II, alluded to the " great circulation ", and Harvey must no doubt have been influenced by the opinions of such men [although the author admits that Harvey makes no mention of Cesalpino in his writings]. In describing the origin of the circulation, Harvey considered the vena cava, and not the heart, to be the fountainhead. There the blood regained its " heat " and " vital spirit " and thus, heated up, it bubbled over into the right auricle, filling it. The Harveian concept of the circulation was therefore: vena cava→lungs→ organs and back to the vena cava. The present author then proceeds to bring this concept up-to-date by introducing his own theory of the circulation of the blood, which he describes at some length [but which has not yet become as famous as Harvey's or part of the history of medicine].

In peroration he admits that all this later work has had its origin and inspiration in the genius of William Harvey, and states that Italy can justly be proud of having so largely influenced the young Harvey during his formative years. *P. I. Reed*

558. **Pirogoff in the Crimean Campaign, 1854–1855**
B. M. FRIED. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **31**, 519–536, July, 1955. 1 fig., 5 refs.

Whereas the medical history of the French and British armies during the Crimean War has received considerable attention, that of the Russian army is very inadequately recorded. Some light is thrown upon conditions in the Russian forces by the letters of the surgeon Nicolai Ivanovich Pirogoff to his wife. This correspondence was published in the original after Pirogoff's death, but has never been translated from the original Russian. In the present paper, after a brief biographical sketch, excerpts from the letters are quoted.

Pirogoff, born in 1810, received a medical education of dubious quality at the University of Moscow. After graduating in 1827 he was fortunately sent for postgraduate work to the better-equipped University of Dorpat, where he specialized in anatomy and surgery and became acquainted with the French and English medical worlds. The years 1833 to 1835, spent at the Charité Hospital in Berlin, disillusioned Pirogoff as to the state of German medicine, and in the latter year he returned to Dorpat as professor of surgery. Six years later he became Professor of Surgery at the Medico-Chirurgical Academy at St. Petersburg and surgeon to the Voenno-Soukhopoutny Hospital. The succeeding years were fruitful in research and in publications on anatomy and surgery, but his attempts to improve conditions at the hospital provoked bitter and corrupt opposition, which eventually enforced his resignation just at the moment when the invading armies set foot in the Crimea. Pirogoff, whose own application was ignored, was awarded a commission only through the intervention of a duchess and sent to besieged Sebastopol.

The Pirogoff letters reveal that, despite its advantage of internal communications, the Russian medical service in the war was as inadequate as that of the enemy. Despite advances in military medicine in the Napoleonic armies, the wounded soldier was still generally regarded by the high command as waste material. The picture portrayed by Pirogoff is one of appalling neglect by an inefficient and corrupt administration. Transport for the casualties was crude and totally insufficient; the wounded accumulated in multitudes in conditions of exposure, filth, and infection; surgical practice was obsessed with extraction of the bullet and with amputation. Pirogoff himself fought hard to improve this state of affairs; he sorted and classified the wounded and continually urged conservative methods of treatment. He was a prime mover in introducing " private " assistance in war, and was helped by a group of female nurses, a number of whom are described in his letters, and whose qualities on the battlefield were as invaluable as those of Florence Nightingale and her assistants. But Pirogoff's attempts to transform the official attitude to military medicine were unavailing in the face of fierce opposition from both the War Administration and the Medical Department.

[It is stated in this paper that rectal anaesthesia was first introduced in 1847 by Pirogoff. In this connexion the claims of a Frenchman, Marc Dupuy, to have made the discovery simultaneously should also be noted. (See *J. Hist. Med.*, 1947, **2**, 379; *Abstracts of World Medicine*, 1948, **4**, 224)]. *F. M. Sutherland*

559. **The Incunabula of the Academy of Medicine.** (Les incunables de l'Académie de Médecine)
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560. **The Study of Medicine in Basle: the Account of a Student of 1668.** (Zum Studium der Medizin in Basel: die Stimme eins Studenten aus dem Jahre 1668)
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561. **The Life of the Medical Student through the Ages.** (La vie des étudiants en médecine au cours des âges)
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